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EXPLORATORY DEVELOPMENT OF AN ULTRAFAST-CURING WOUND DRESSING

ANNUAL/FINAL REPORT

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A drug-dispensing field dermal dressing has been developed. The dermal dressing, which can be easily applied by an untrained person, contains antimicrobials to prevent bacterial infection. The medicated dermal dressing is made of an ultra-fast curing polyurethane oligomer which is designed to cure at room temperature and delivers drugs on a controlled, sustained and highly reproducible basis.

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Karen Wasse June 17, 1991
PI Signature Date

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INTRODUCTION

This report summarizes research conducted on the contract DAMD17-88-8012 supported by USAMRDC, over the past three years directed towards developing antimicrobial dermal dressings (ADDs'). The dressings consist of a trilaminate composed of an outer medical grade polyurethane fabric, an acrylic-based pressure sensitive adhesive, and an antimicrobial impregnated polyurethane laminate which serves as a controlled drug release layer. The objectives in developing this new technology have been to create a medicated dressing that is:

(1) easily applied under adverse climatic conditions,

(2) highly compliant and abrasion resistant and

(3) allows controlled release of antimicrobial agents over a seventy two hour period against a variety of microbial organisms.

The new dressing is capable of incorporating heat labile antimicrobial agents and releasing them in a controlled fashion when in contact with the wound. This was made possible by the development of a room temperature, rapid ultraviolet (UV) curable liquid polyurethane oligomer. The liquid mixture of urethane and drugs is cured under UV lights and the resultant monolithic film provides controlled release of the agents when placed on the wound. This targeted drug delivery minimizes many of the inherent problems associated with conventional systemic drug delivery.

The three year research program had been directed towards development of dressings which would be effective against a wide range of microorganisms. Several types of dressings were developed and tested; of these, two types of dressings were chosen for conducting preliminary shelf stability testing:

(1) a dressing containing 30% chlorhexidine gluconate; and

(2) a dual loaded dressing containing 20% silver sulfadiazine and 10% chlorhexidine gluconate.

Successful completion of all the proposed tasks during the course of the three years, has involved making the base oligomer, developing fabrication methods, developing methods to measure the antimicrobial agents, monitoring elution kinetics, optimizing drug release and supplying USAIDR with sterile dressings for in vivo evaluation of the technology.

The work resulted in the development of new techniques for drug analyses, improved fabrication methods for sustained release and better management of wound healing. Work in the latter portion of the contract was devoted to preliminary shelf stability testing. The final formulations were subjected to accelerated conditions for six months. The following report provides a detailed description of the studies carried out in the performance of this program.

BACKGROUND

The study of the environmental conditions under which the process of wound healing takes place is relatively recent. The process of wound repair and healing was known to consist of a chronological sequence of events (1). There was also an awareness that an open wound was subject to the threat of infection. Early studies showed that optimal wound healing occurred under a scab. As a result, dressings were used to protect the wound site from bacterial invasion and infection.

Research in the late sixties and early seventies showed that the optimum conditions for wound healing occurred under a dressing that maintained a moist environment (2). The development of the polyurethane products (a temporary artificial skin) for wound dressings arose from the attempts to provide a moist environment much like nature's blister (3).

Prior to the studies on the potential effects of dressings on the wound repair process, the medical community had thought that the surgical dressing mainly absorbed exudate, cushioned the wound site, and hid the site from the patient. This research illustrated that dressings can affect the response to the wound and even retard healing through dehydration or tissue damage during removal. Dressings can optimize epithelialization, reduce pain (which is associated with wound dehydration), and minimize local

inflammation. The dressings impregnated with drugs can also deliver medication (4).

Optimal wound healing occurs when the dressing material strikes a balance between dehydration and maceration (which results from accumulation of excess exudate). In addition to stimulating pain, dehydration leads to desiccation and cell death, undermining epithelial movement and wound closure. Prevention of dehydration can minimize eschar formation and inflammatory response. Maceration, which is stimulated by excess fluids and debris, is often accompanied by bacterial proliferation which retards the wound healing process (5).

Currently available wound dressings are primarily limited to gauze pressure bandages. These materials have minimal beneficial characteristics. The dressing materials function as simple coverings that are not impervious to microorganisms, thereby providing little protection from infection. By being absorbent, these dressings may desiccate the wound thus delaying healing. The material absorbed into the dressing may provide an ideal substrate for supporting microbial growth. These materials may also provide a mild degree of hemostasis via the application of pressure. However, pressure must be maintained for long periods.

The desired balance between dehydration and maceration has had a direct impact on the development of synthetic dressings. The

moist healing environment (to counter dehydration) has been the primary goal of materials development. Permeability to vapor (to counter maceration) has been an influential factor in the development of most of the materials.

One of the most successful commercial dressing for split-skin graft donor sites and burn care is Op-Site^{R} (Smith & Nephew). Op-Site is a polyether-based, moisture-vapor permeable polyurethane membrane compounded with silica gel. The polyurethane membrane is hydrophilic, and is coated at the edges with a polyvinyl ethyl ether adhesive (6). Op-site has been shown to offer significant advantages over conventional dressings in the management of superficial injuries, split-skin graft donor sites, and burn sites (6):

A) the hydrophilic polyurethane dressing protects wounds from bacterial contamination, while providing a suitable environment for rapid wound healing;

B) patients seem more comfortable with the polyurethane dressing than with standard bandages; and

C) rapid healing is produced by enhancement of re-epithelialization through increased mitotic division and migration of epidermal cells.

However, Op-Site has several disadvantages:

1) it is not amenable for self application;

2) it adheres tenaciously to both intact skin and the scab. During

removal, not only is the patient subjected to acute localized pain, but the wound site frequently starts rebleeding when the scab is forcibly disturbed; and

3) it is non-medicated.

The new wound dressing developed at TCI is a self-adherent, medicated dressing capable of being applied to the wound by the injured individual. This wound dressing is fabricated from a UV curable polyurethane and can incorporate antibiotics or antimicrobials. The release of drugs from the dressings is controlled to last at least 72 hours. Figure 1 illustrates a cross section of the TCI Antimicrobial Dermal Dressing (ADD), showing the liner reflected back, exposing the antimicrobial loaded controlled release layer. The backing material is made of a flexible, nylon reinforced semi-permeable polyurethane membrane.

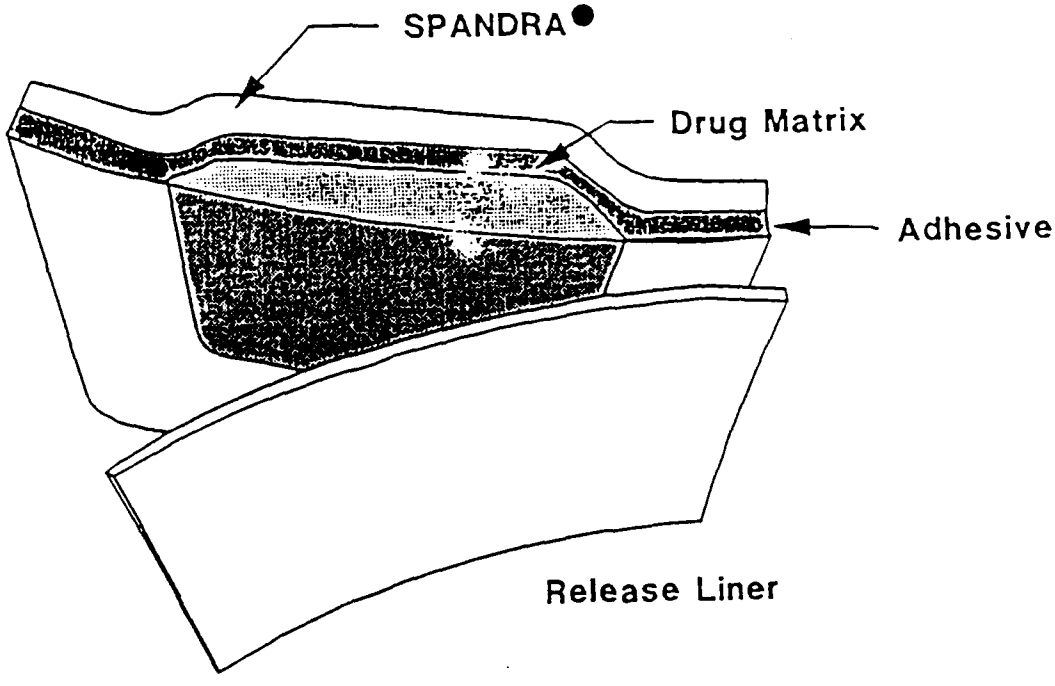


Figure 1. Cross Sectional Illustration of the TCI Antimicrobial Dermal Dressing with the Antimicrobial Controlled Release Layer Exposed.

SUMMARY OF WORK PERFORMED

The research was performed as tasks over the three years of the contract. The several tasks performed during each year are briefly described here.

A major task for Year 1 was the synthesis and manufacture of the UV curable polyurethane oligomer. The vinyl terminated urethane oligomer was synthesized from three reactants: isophorone diisocyanate, polypropylene glycol and hydroxyethyl methacrylate. The photoinitiator was added to this finished product to produce the UV curable property. Once the formulation was identified, ample quantities of the oligomer were produced at the beginning of each contract year to complete the work load.

The wound dressings tested in vivo, on guinea pigs at USAIDR laboratories exhibited a tendency to adhere to the wound. Removal often resulted in the dislodging of blood clots and bleeding. However, the use of a silicone gum or fluid in the dressing helped to prevent this adhesion. The silicone fluid when incorporated into the oligomer migrated to the surface and formed a nonadhesive film which facilitated easy removal of the dressing. The purpose of task 2 was to identify the loading of silicone fluid in the oligomer required to prevent adhesion to the wound. Various levels of low viscosity medical grade silicone fluid (Dow Corning DCO 200) ranging from 2% to 5% by weight were incorporated into the

oligomer. The results of the ensuing tests demonstrated that the 2% load of silicone fluid was sufficient to provide the adequate degree of release (7).

The dressing is attached to the skin by means of an adhesive. The selection of this adhesive was based upon several factors namely:

(1) adhesivity to skin
(2) cohesive strength
(3) shear strength
(4) irritancy and
(5) shelf stability.

Thirty dressings incorporating varying quantities of silicone were tested for adhesive characteristics by USAIDR and these results were reported (7).

Wound dressings should allow the permeation of gases but at the same time provide a moisture barrier. The backing material used to fabricate the wound dressing was tested for its permeation characteristics and these results were reported (7).

The next phase in the development of the wound dressing was the incorporation of suitable antimicrobial agents. Two antibiotics, gentamicin sulfate and clindamycin phosphate were the initial drugs of choice. These two antibiotics were incorporated into the oligomer and fabricated into dressings. These dressings

were tested for release kinetics in vitro using Franz diffusion cells. Methodology was developed for the analysis of each antibiotic. The maximal loading was established, and the dressings incorporating this load were tested by USAIDR in vivo to establish efficacy parameters under task 5.

Eleven tasks were successfully completed during the second year. Task 1 of Year 2 focused on optimizing the release of the antibiotics from the dressing as well as adhesion to the skin. Several innovative techniques were utilized to optimize the efficiency of the wound dressing namely:

(1) improve dispersion of the drugs in the matrix

(2) increasing the potency of the antibiotics

(3) increasing contact surface area

(4) increasing hydrophilicity and

(5) increasing the thickness of the dressing.

These techniques were evaluated in vitro and the optimized dressings were tested at USAIDR (8).

The adhesive tested in Year 1, though very aggressive on dry skin, was not effective on moist or wet surfaces. The adhesive had to adhere to moist skin, since the wound dressing was required to be used under all climatic conditions. Several types of adhesives were tested for their wet and dry strength and a suitable candidate was chosen (8). This adhesive was used for all subsequent formulations tested by USAIDR.

Dressings incorporating several different formulas were fabricated and tested at TCI. The in vitro tests resulted in the development of new and/or modified analytical techniques for the analysis of the antibiotics (8). Five formulations incorporating gentamicin sulfate and clindamycin phosphate were fabricated for testing in vivo at the USAIDR facility in Maryland. These dressings were also extracted for residual drug content after application on wounded guinea pigs.

The antibiotics used in the wound dressings are very potent. However, these agents are specific in their bacteriocidal action and have no activity against fungi. The in vivo tests conducted on guinea pigs demonstrated the specific spectrum of activity of each antibiotic. The specificity limited the use of these drugs as universal candidates for dressings. Hence the shelf stability of the dressings incorporating these antibiotics was not assessed.

Other suitable agents had to be chosen for incorporation into the dressing matrix. A candidate of choice was chlorhexidine gluconate, a wide spectrum antimicrobial solution with bacteriocidal and fungicidal properties. Lyophilization techniques assisted the incorporation of this drug into the polymer matrix. The effective use of formulating principles optimized the release of chlorhexidine gluconate from the dressing (9). In vitro microbiological plate assays helped demonstrate the efficacy of these dressings. Five formulations incorporating lyophilized

chlorhexidine gluconate were tested on guinea pigs by USAIDR. The optimal formulation was selected for testing shelf life.

Microbiological plate tests are a useful tool in establishing the effectiveness of an antimicrobial agent against specific strains of microorganisms. These techniques were employed to select an agent, or a combination of agents, for incorporation into the wound dressing to combat a broader microbial spectrum (9).

Based on the microbiological plate tests, a dually loaded dressing incorporating silver sulfadiazine and chlorhexidine gluconate was selected, as well as a triple loaded combination incorporating these two agents along with clindamycin phosphate. The agents were successfully incorporated into the polymer and prepared for subsequent testing.

The successful development of several prototype formulations resulted in the initiation of the last phase of the contract. Two prototype formulations were selected and the exploratory shelf stability studies performed. The shelf stability was performed under accelerated conditions so that a reasonable prediction of shelf life could be obtained.

EXPLORATORY SHELF STABILITY STUDIES

Degradative chemical reactions in formulations take place at definitive rates. They depend on such conditions as concentration of reactants, temperature, pH, radiation, etc. An effective and efficient study of these reactions by the application of physicochemical principles has made it possible to predict the stability of a drug product at normal shelf storage conditions from drug products stored under exaggerated conditions.

The evaluation of temperature dependency of a formulated product is useful to determine the rate of degradation. This permits the prediction of stability for the product at ordinary shelf temperatures from accelerated conditions. The most commonly used method for expressing the influence of temperature on chemical reaction is the relationship proposed by Arrhenius (10).

The utility of the temperature dependency relationship depends on the controlling mechanism of the degradation process. In solutions, there is a considerable change in the heat of reactions at elevated temperatures. This makes the mathematical prediction very reliable. On the other hand, where the heat of activation is very small, the effect of temperature is negligible and use of the Arrhenius predictions can be erroneous.

Graphic methods, based on the Arrhenius principles are more

simplistic and can be used under a wide range of conditions. Several graphic techniques have been employed to predict the breakdown that may occur over prolonged periods of storage at normal shelf conditions (11). One of the popular methods plots the fractional life period or the time required for the drug to decompose to a fraction of the original potency, versus the reciprocal of the absolute (K) temperatures. The time for the degradation or reduction in concentration at several temperatures to reach a predetermined theoretical potency is noted. These log time values at several temperatures are plotted and the time for the concentration to reach this point at room temperature can be obtained from the resulting straight line by extrapolation.

The performance of the tasks during the three years of the contract resulted in the development of two prototype formulations. The final phase of the program was initiated after the prototype formulations were selected. This phase required the manufacture and fabrication of large quantities of ADDs'. The batch sizes for tasks VI and X had to be 3 to 4 times larger than the batch sizes for tasks IV and VIII. Five hundred ADDs' each, of 30% loaded chlorhexidine gluconate as well as the dual combination containing 20% silver sulfadiazine and 10% chlorhexidine gluconate were fabricated, hermetically packaged and sterilized by radiation techniques. An exploratory stability study was performed on these prototype ADDs'. A group of forty-eight randomly sampled ADD's from each of the two prototype formulations were placed under each of

the five conditions specified below:

(1) 45^0 C, 90% R.H,

(2) 38^0 C, 90% R.H,

(3) Room Temperature

(4) 23^0 C, under water,

(5) -40^0 C.

The dressings from each of these two batches (Batch Nos. 008081-PDDS1 - 30% chlorhexidine gluconate and 010181-PDDS2 - 20% Silver sulfadiazine and 10% chlorhexidine gluconate) were tested for in vivo efficacy by USAIDR at the beginning of the six month period to establish baseline parameters. The in vitro testing was performed every two months for six months for each of the ADDs' and the results of these tests are reported here. At the end of the six month period, the dressings exposed to the several conditions were delivered to USAIDR for in vivo evaluation.

1. Chlorhexidine gluconate ADDs'

The chlorhexidine gluconate ADDs' incorporated 30% lyophilized chlorhexidine gluconate powder in the polymer matrix. The stability of these chlorhexidine gluconate ADD's was determined using two methods:

1. analyzing the drug for the presence of p-chloroaniline (PCA) a degradation product, and
2. measuring the maximum amount of chlorhexidine gluconate

eluted from the ADD's over 72 hours.

The second method for determining storage stability involves an analysis of elution data acquired from ADD's removed from each of the storage conditions. The elution kinetics were recorded documenting the initial time point (t = 0) for the samples undergoing accelerated shelf stability. The elution kinetics of the samples subjected to the accelerated conditions at the 2, 4 and 6 month intervals were then compared to the samples at time t = 0.

2. Dual Loaded ADDs'

The dual loaded ADDs' incorporated 20% micronized silver sulfadiazine and 10% lyophilized chlorhexidine gluconate in the polymer matrix. The stability of these ADDs' was determined for each of the two antimicrobial agents separately. The stability profile of the lyophilized chlorhexidine gluconate was determined by the methods used for the single loaded ADD incorporating chlorhexidine gluconate. The silver sulfadiazine concentration in the ADDs' was determined by the drug elution rate profiles (9). This HPLC assay is the only method available for the determination of silver sulfadiazine, though it does not determine the concentration of free silver caused by drug degradation. However, silver sulfadiazine has been shown to be stable for at least two years in the solid state (12).

Results

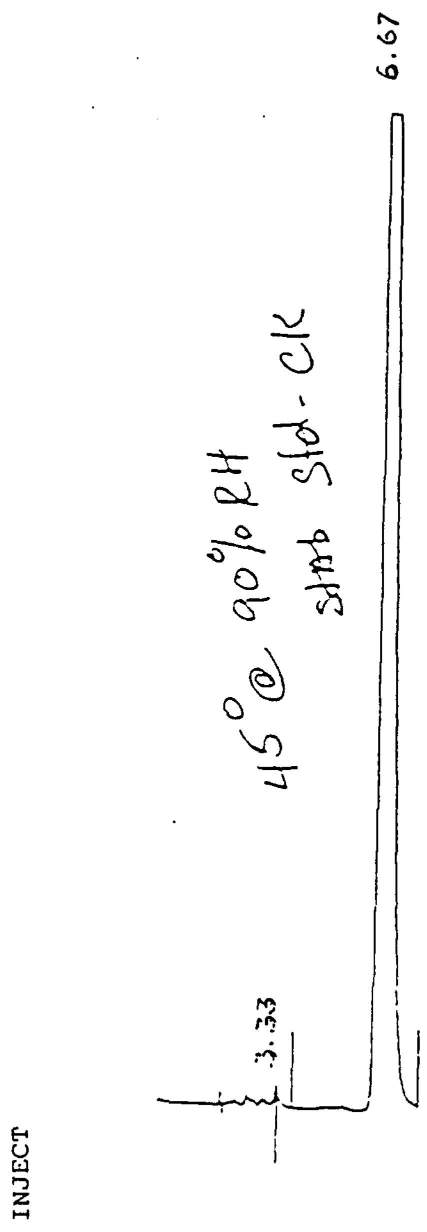
1. Chlorhexidine gluconate ADDs'

The chlorhexidine gluconate ADD's were subjected to quality control tests. The accelerated stability tests conducted showed that chlorhexidine gluconate is stable even when stored at 45^0 C for six months. Results of the assay showed p-chloroaniline to be under 10 mcg/ml; Figure 2 represents a chromatogram depicting this result. Figure 3 represents a chromatogram of a 1000 mcg/ml chlorhexidine gluconate standard spiked with p-chloroaniline. A comparison of these two chromatograms confirmed that chlorhexidine gluconate stored at 45^0 C for six months exhibits very little degradation products; the maximum PCA recorded was less than 10 mcg/ml.

The chlorhexidine dressings exhibited efficacy in the microbiological zone of inhibition testing and complied to the sterility tests at the end of the six (6) month storage period; these results along with the certificate of analysis, are appended (Appendix II).

The baseline release profile (t = 0) of the chlorhexidine ADD's is shown in Figure 4. Figures 5, 6 and 7 illustrate data obtained for the ADD samples subjected to the accelerated conditions (-40^0 C, 23^0 C under water, ambient, 38^0 C and 45^0 C) at

2, 4 and 6 month intervals respectively. The tabulated results for the dressings are summarized in Appendix III.



FEB. 23, 1991   15:43:47   CHART 0.50CM/MIN
RUN #93   CALC #0
COLUMN   SOLVENT   OPR ID 6

EXTERNAL STANDARD QUANTITATION

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TOTAL 11711.00000

Figure 2. Chromatogram of Lyophilized Chlorhexidine Gluconate Stored at 45°C for Six Months

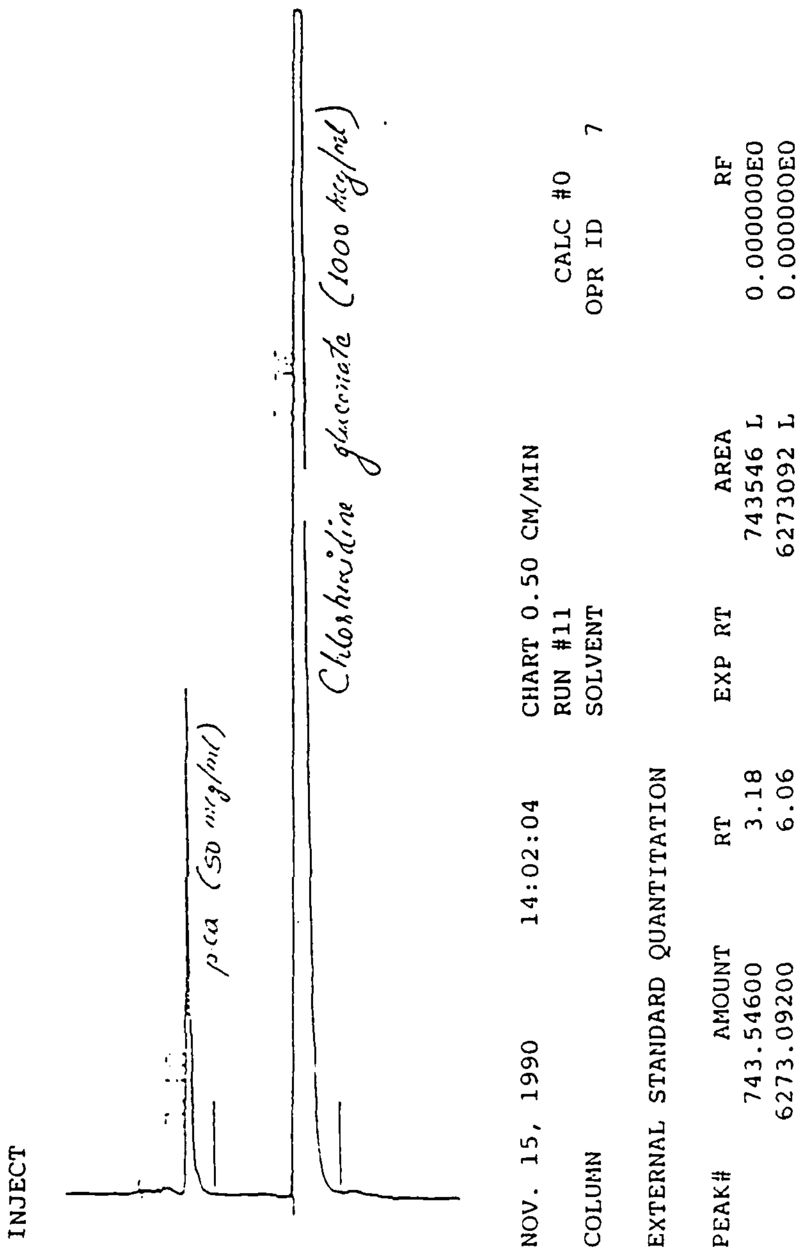


Figure 3. Chromatogram of Chlorhexidine Gluconate Standard (1000 mcg/ml) Spiked with p-chloroaniline (50 mcg/ml).

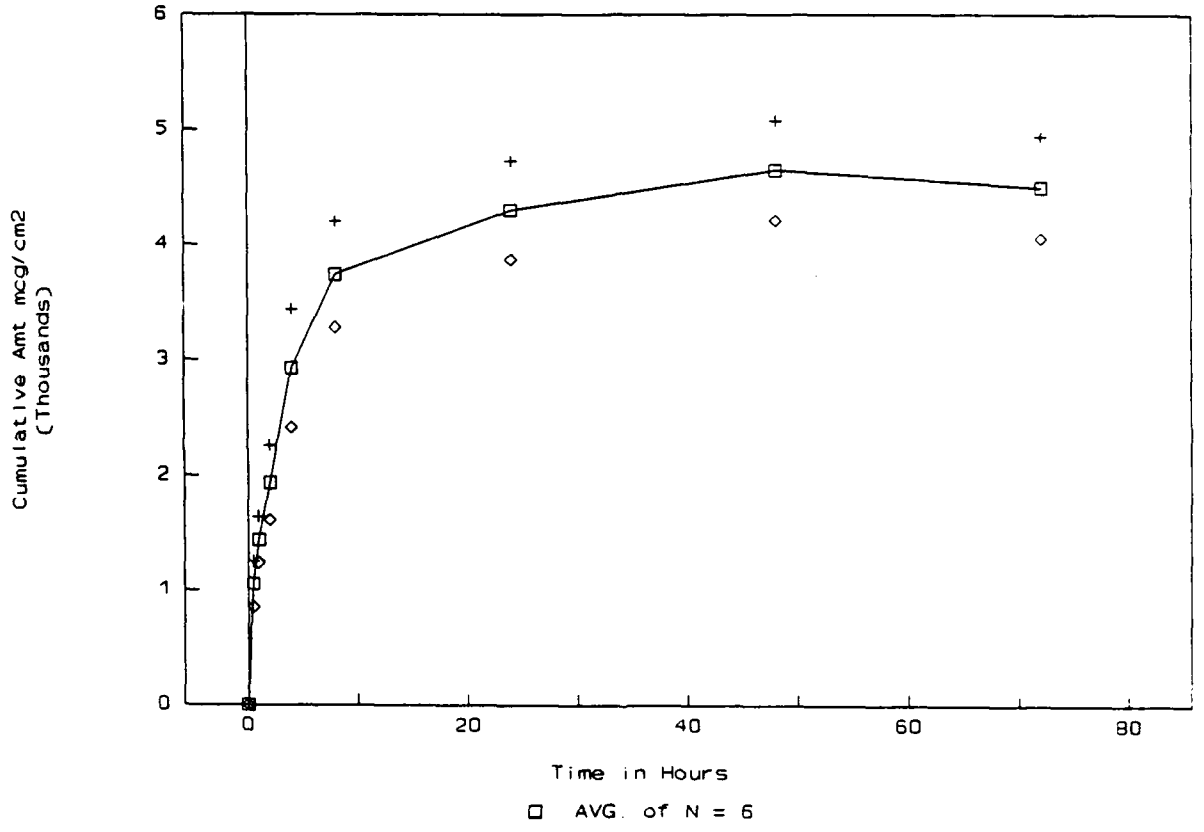


Figure 4. Release Profile of 30% Chlorhexidine Gluconate ADD's After E-beam Sterilization. Stability Samples at Time t = 0.

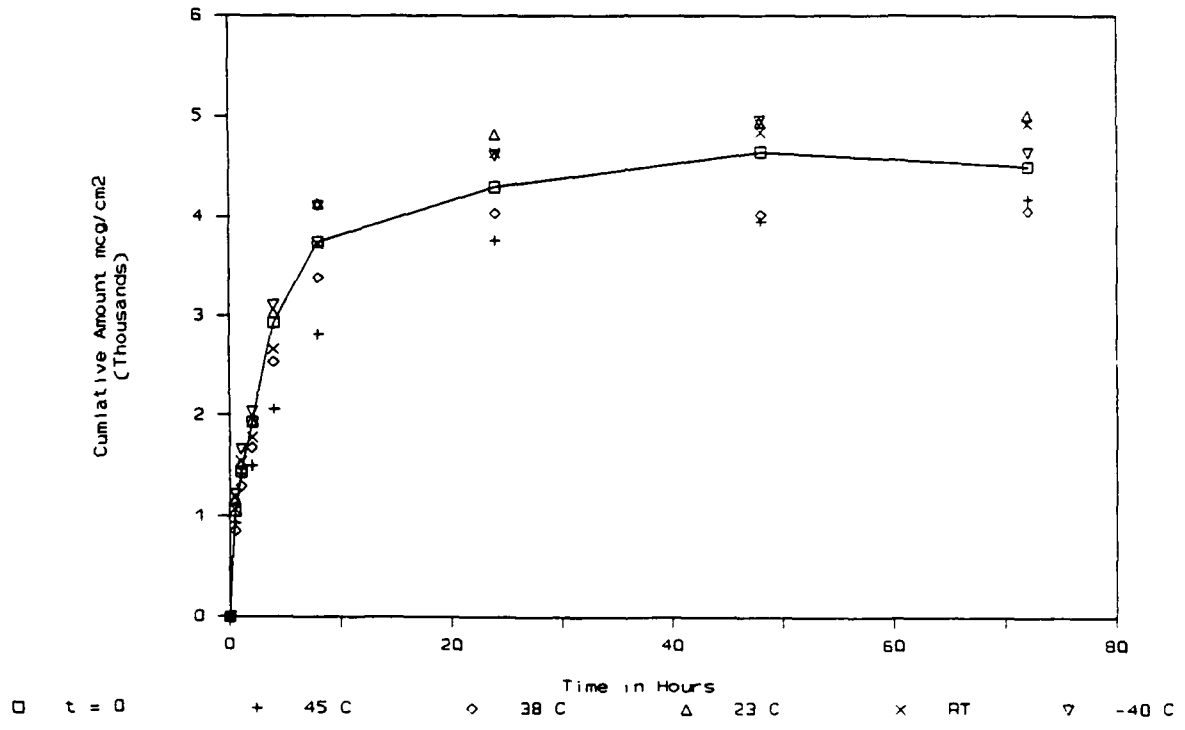


Figure 5. Release Profile of 30% Chlorhexidine Gluconate ADDs' Subjected to Accelerated Storage Conditions at 2 months.

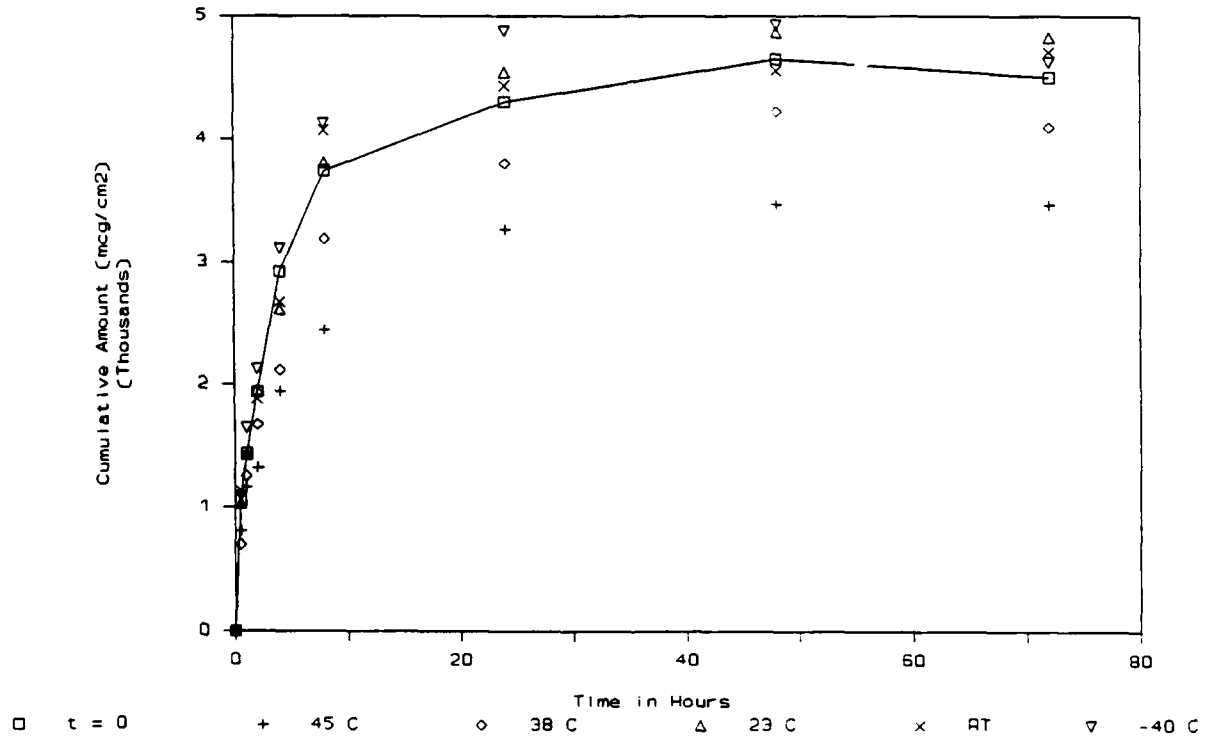


Figure 6. Release Profile of 30% Chlorhexidine Gluconate ADDs' Subjected to Accelerated Storage Conditions at 4 months.

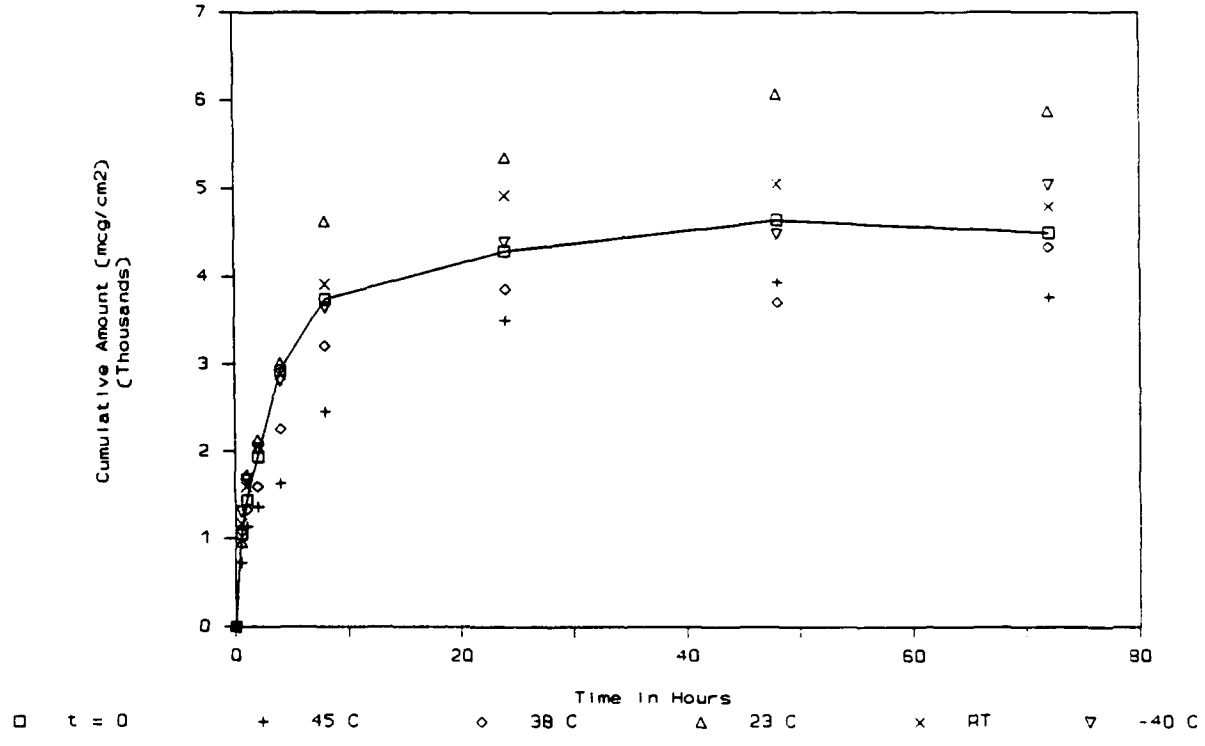


Figure 7. Release Profile of 30% Chlorhexidine Gluconate ADDs' Subjected to Accelerated Storage Conditions at 6 months.

2. Dual Loaded ADDs'

The dual loaded ADDs' were subjected to various tests in the laboratory (9). The ADDs' subjected to higher temperatures were noticeably dark in color on visual inspection. The elution rates for the silver sulfadiazine portion was also higher. However, the chromatographic analysis of the eluates demonstrated no detectable degradation of the chlorhexidine gluconate content. Figures 8 and 9 illustrates the baseline release profiles for the dual loaded ADD's at time t = 0, for chlorhexidine gluconate and silver sulfadiazine respectively.

Figures 10, 12 and 14 illustrate the elution profiles of chlorhexidine gluconate from the ADDs' at 2, 4 and 6 month intervals. Figures 11, 13 and 15 illustrate the elution rate profiles for the silver sulfadiazine from the dual loaded ADDs' at 2, 4 and 6 month periods. The tabulated results are included in the Appendix.

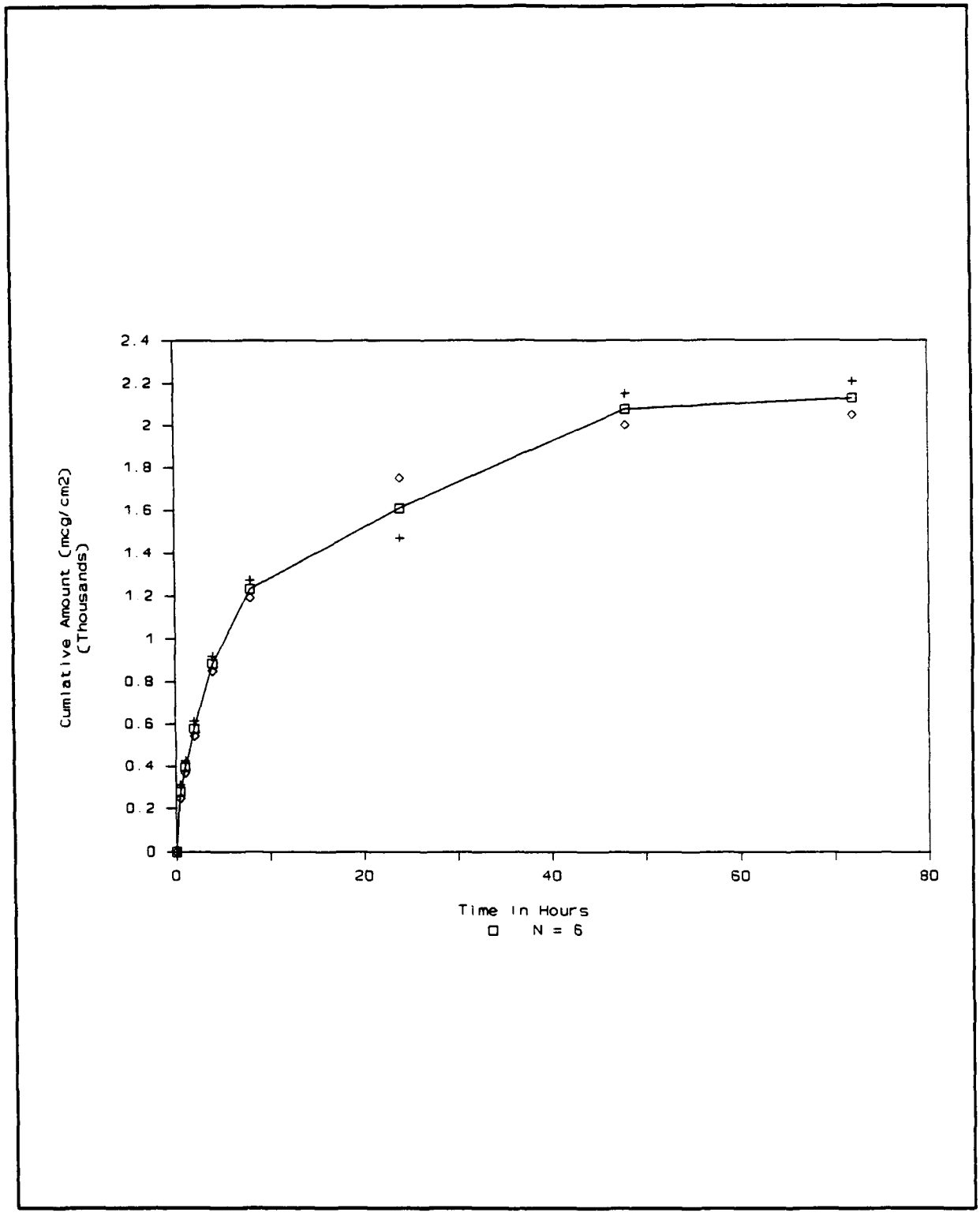


Figure 8. Release Profile of Chlorhexidine Gluconate from the Dual Loaded ADDs' at t = 0.

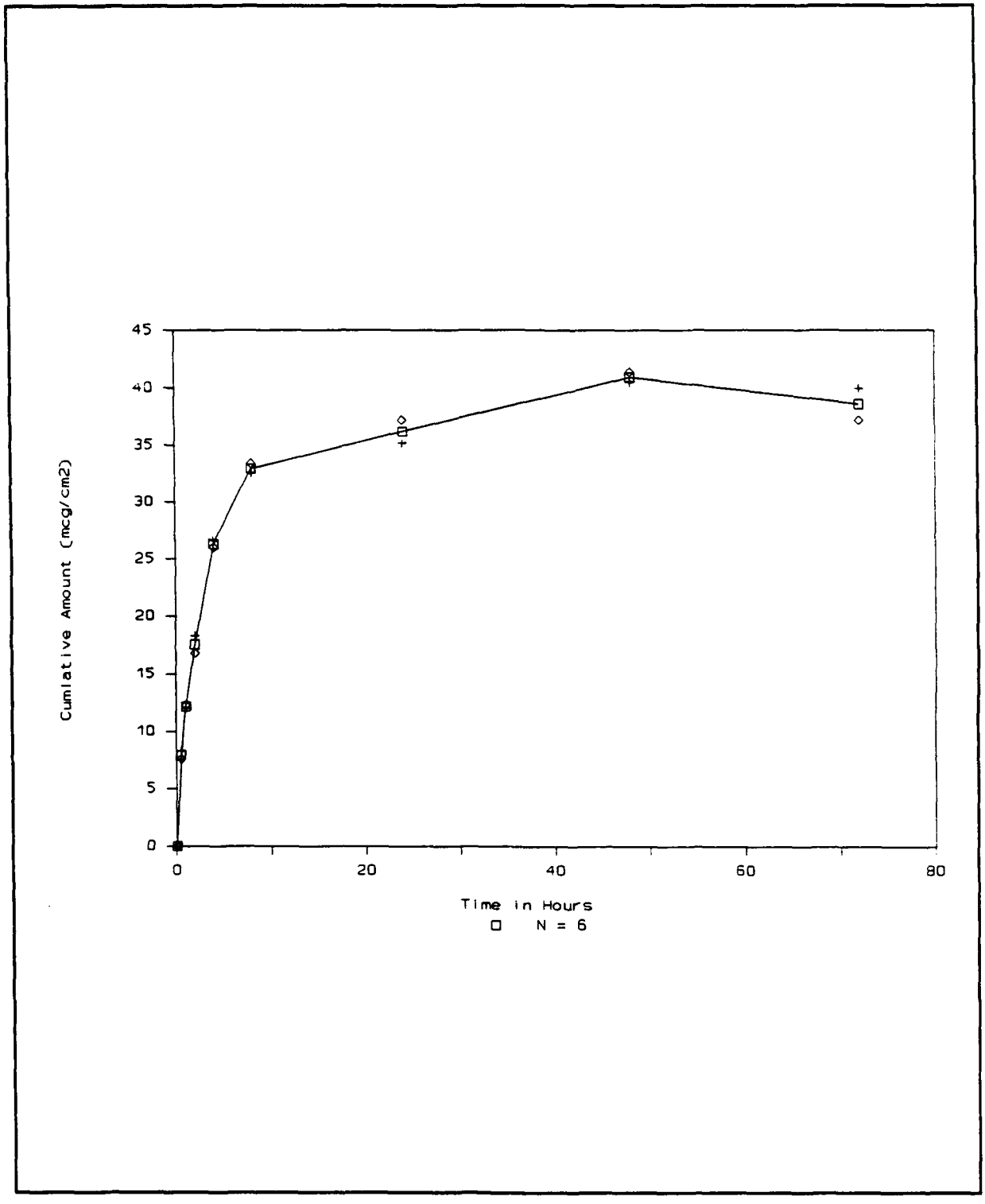


Figure 9. Release Profile of Silver Sulfadiazine from the Dual Loaded ADDs' at t = 0.

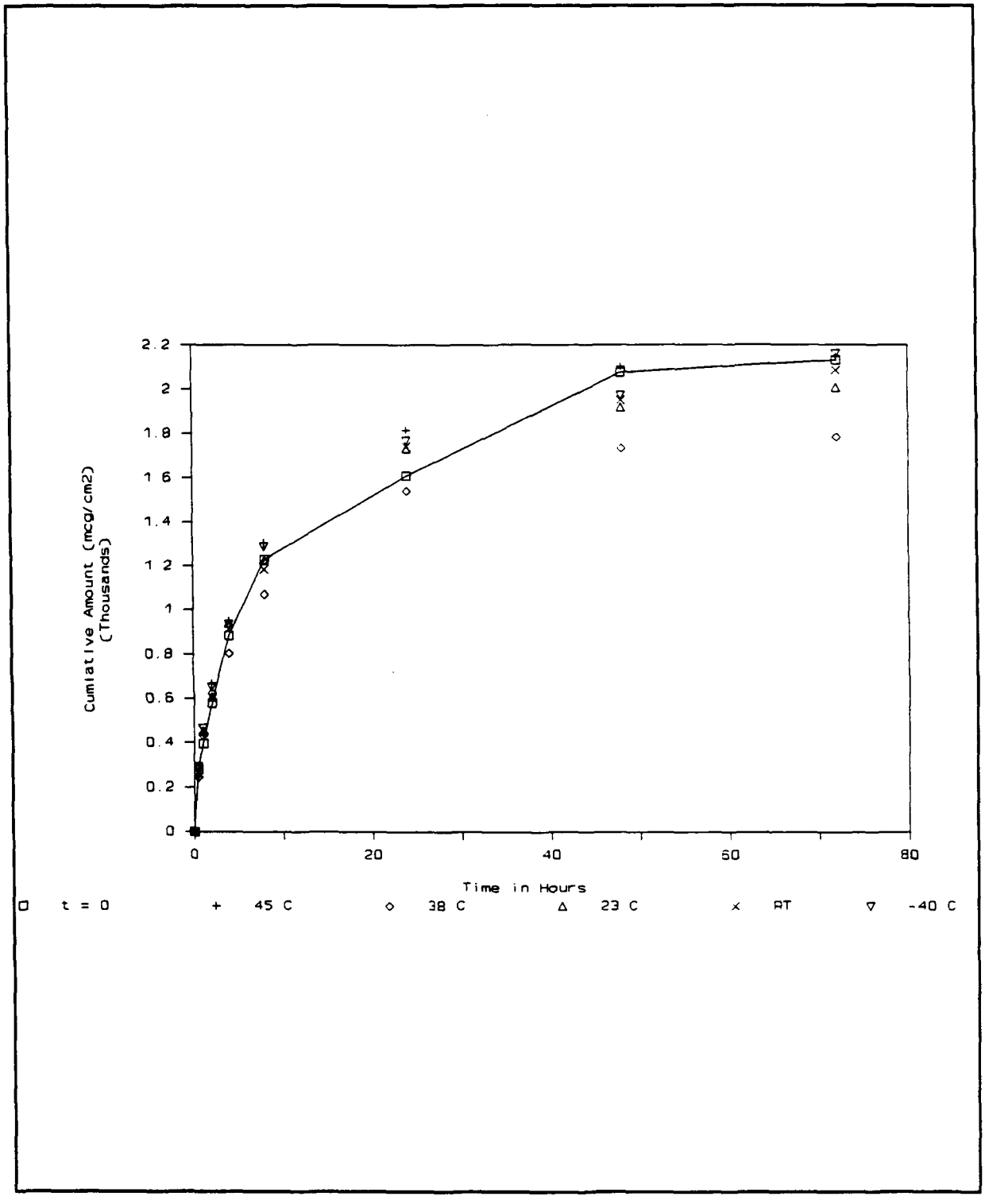


Figure 10. Release Profile of Chlorhexidine Gluconate from the Dual Loaded ADDs' at t = 2 months.

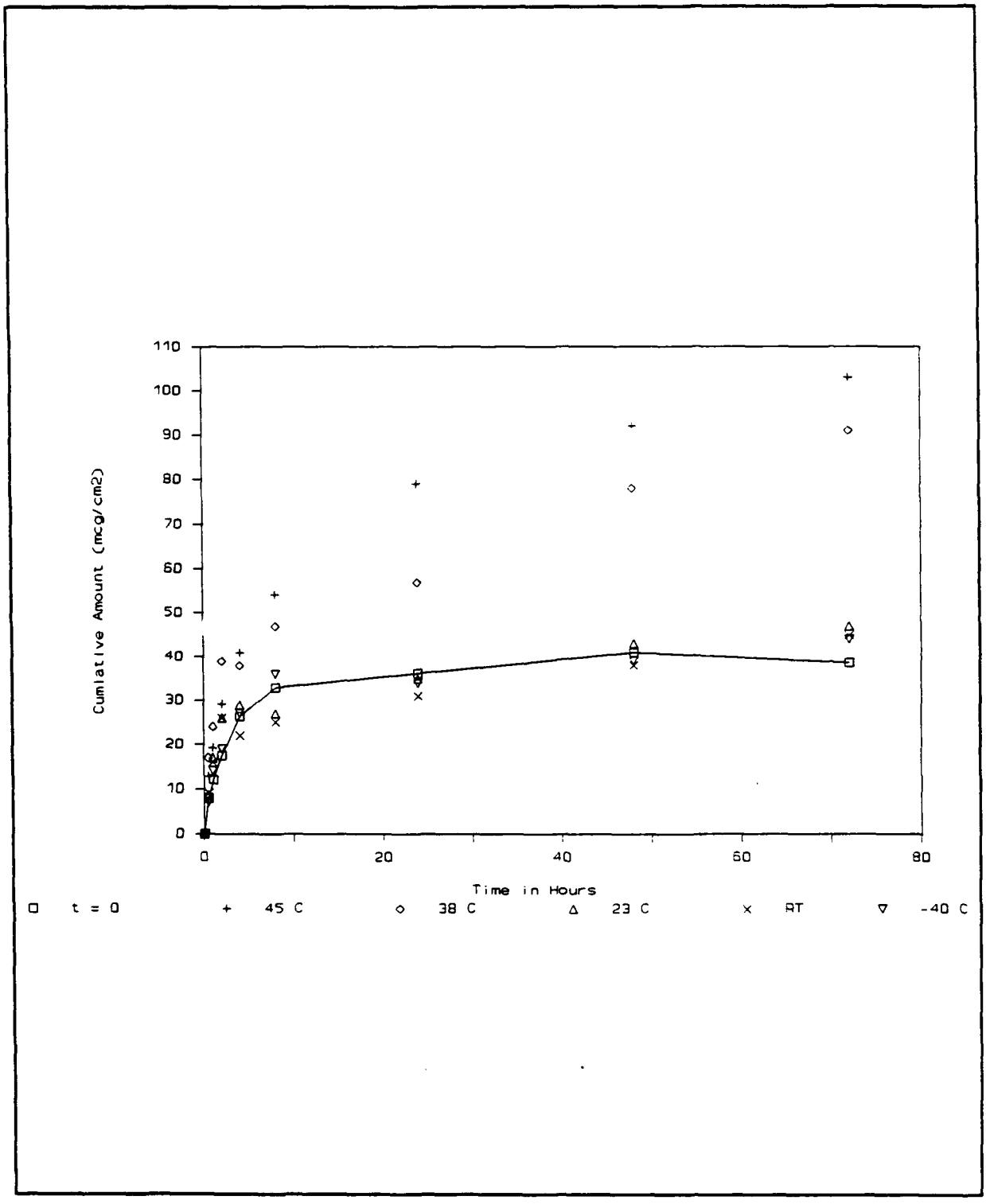


Figure 11. Release Profile of Silver Sulfadiazine from the Dual Loaded ADDs' at t = 2 months.

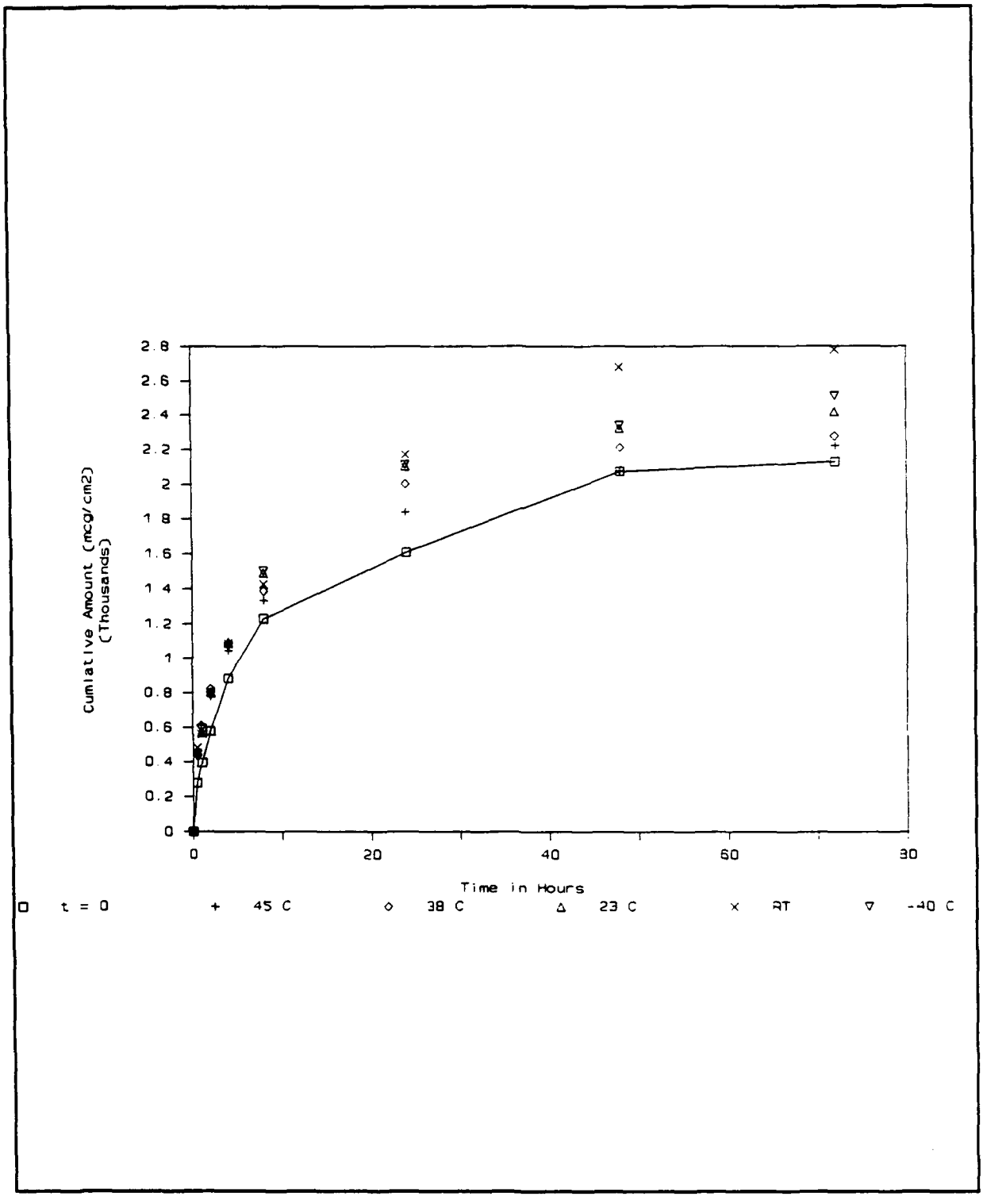


Figure 12. Release Profile of Chlorhexidine Gluconate from the Dual Loaded ADDs' at t = 4 months.

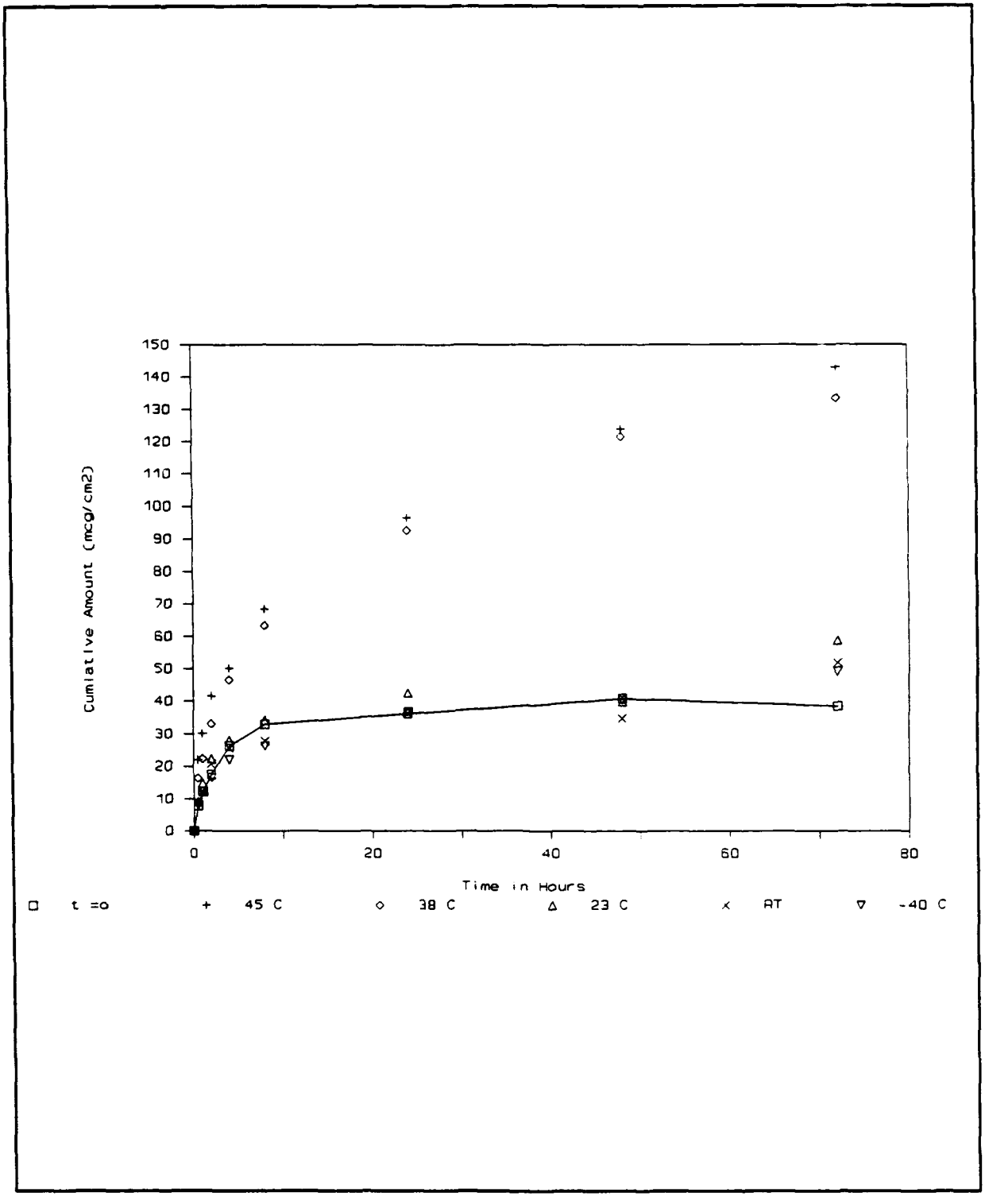


Figure 13. Release Profile of Silver Sulfadiazine from the Dual Loaded ADDs' at t = 4 months.

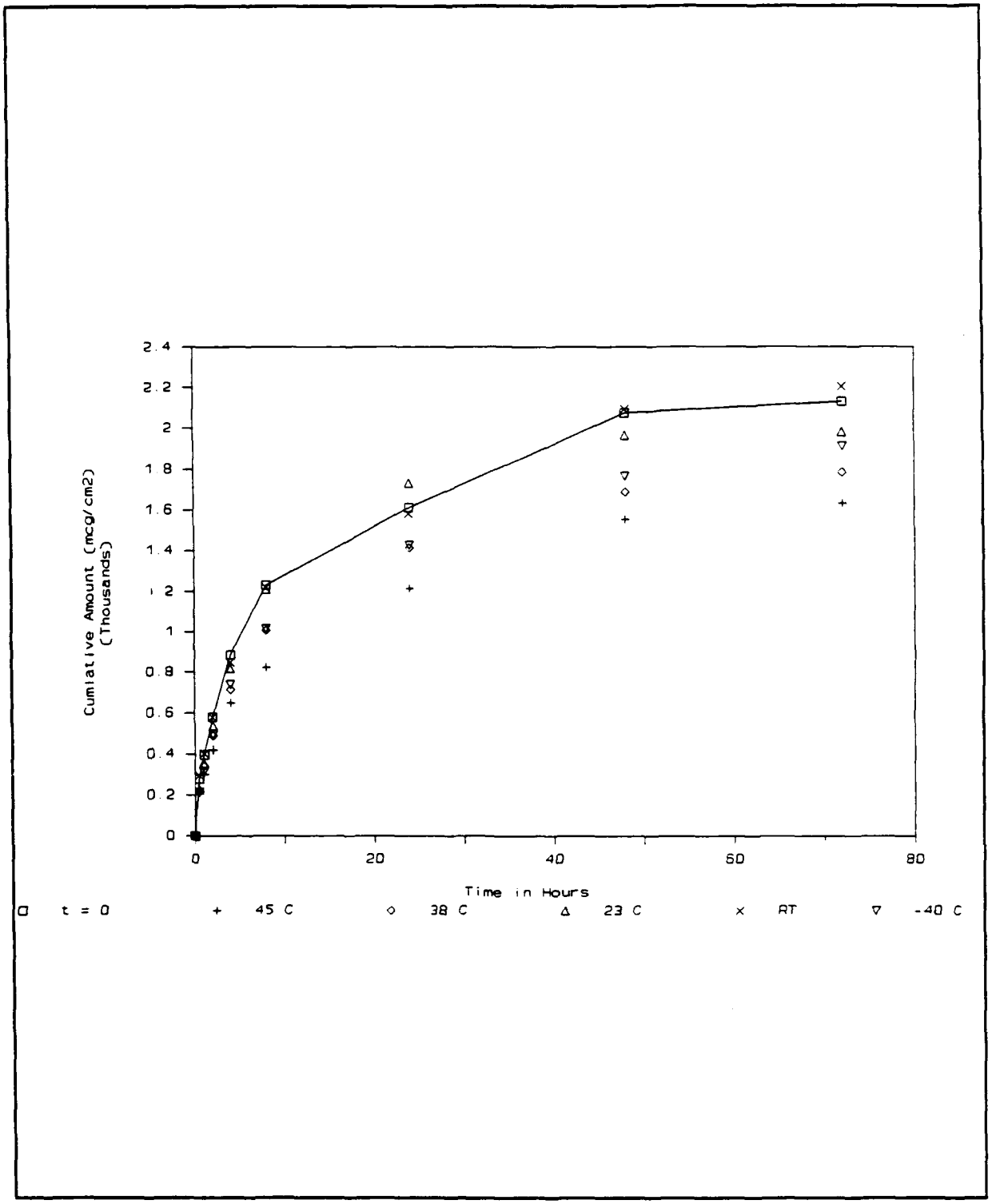


Figure 14. Release Profile of Chlorhexidine Gluconate from the Dual Loaded ADDs' at t = 6 months.

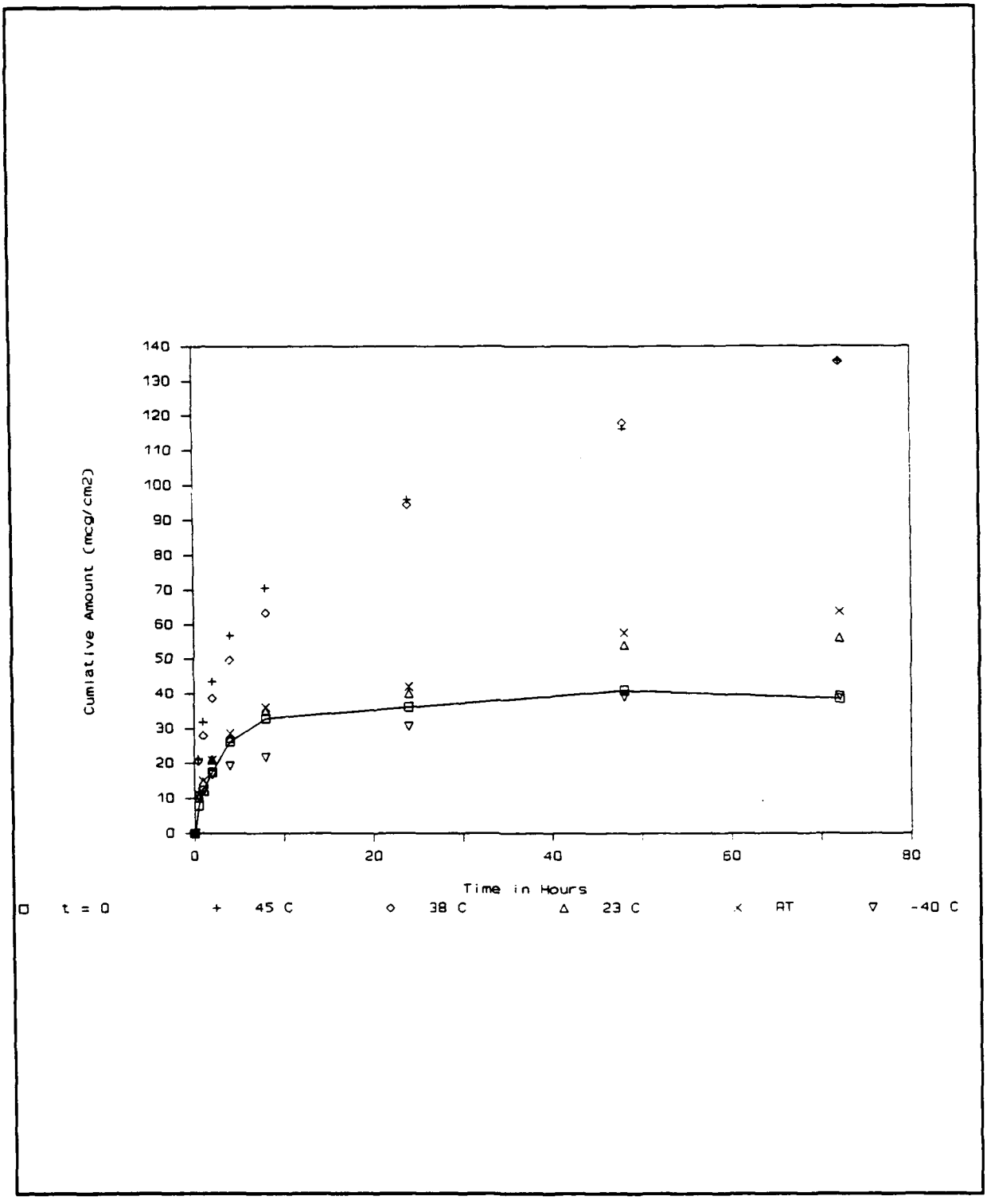


Figure 15. Release Profile of Silver Sulfadiazine from the Dual Loaded ADDs' at t = 6 months.

Discussion

The chemical stability of chlorhexidine gluconate was tested using chromatographic techniques. Chlorhexidine gluconate was found to be 99.5% stable even when stored at high temperatures. Since the degradation reaction was negligible, the release of the drug from the polymer matrix over a period of time became the determining factor.

The graphical method was adopted for predicting the shelf stability of chlorhexidine gluconate ADDs'. It was hypothesized that to demonstrate in vivo efficacy, the in vitro release profile of the ADD should show at least 3000 mcg/sq. cm. after 72 hours. This was considered to be the minimum effective concentration (MEC) of the drug to be released in vitro, for the ADDs' to be effective in vivo. This was determined from the in vivo trials conducted earlier (9). The 6 mil thick dressing (Formulation 2) demonstrated effectiveness when tested on guinea pigs. This dressing released approximately 3000 micrograms/sq. cm. in 72 hours or about 64% of the 12 mil dressing tested for shelf stability (Figure 16). This in vitro release profile of the 6 mil thick ADD (or 64% of 12 mil samples at t = 0) was used as the MEC of the drug to be released from the dressing.

The elution profiles of the ADDs' subjected to the varying storage temperatures at periodic intervals were then plotted

(Figures 4, 5, 6 & 7). Figure 17 compares the elution rates of the ADD's at t = 0, to those stored at 45^{0}C and -40^{0}C for 2, 4 and 6 months. The ADD's stored at -40^{0}C show no change in the elution rates over the control (t = 0). The ADD's stored at elevated temperatures (45^{0}C), show a decrease in the elution rates. The logarithmic percent of the cumulative amount of the drug released from the ADDs' compared with those of the ADDs' at time t = 0, was plotted against time in days (Figures 18, 19, 20 and 21). The time for the concentration to fall to 3000 micrograms per square centimeter of the original concentration was then read from the graphs generated using trend analysis of Harvard Graphics software program. The log time to 3000 mcg/cm^2 was then plotted against 1/T, and the extrapolation from 25^{0}C (3.36 x 10^3) to the time (Y axis) predicts the shelf life of the product in days (Figure 22). The shelf life of the ADDs' stored under normal conditions was estimated to be about 800 days or over two years.

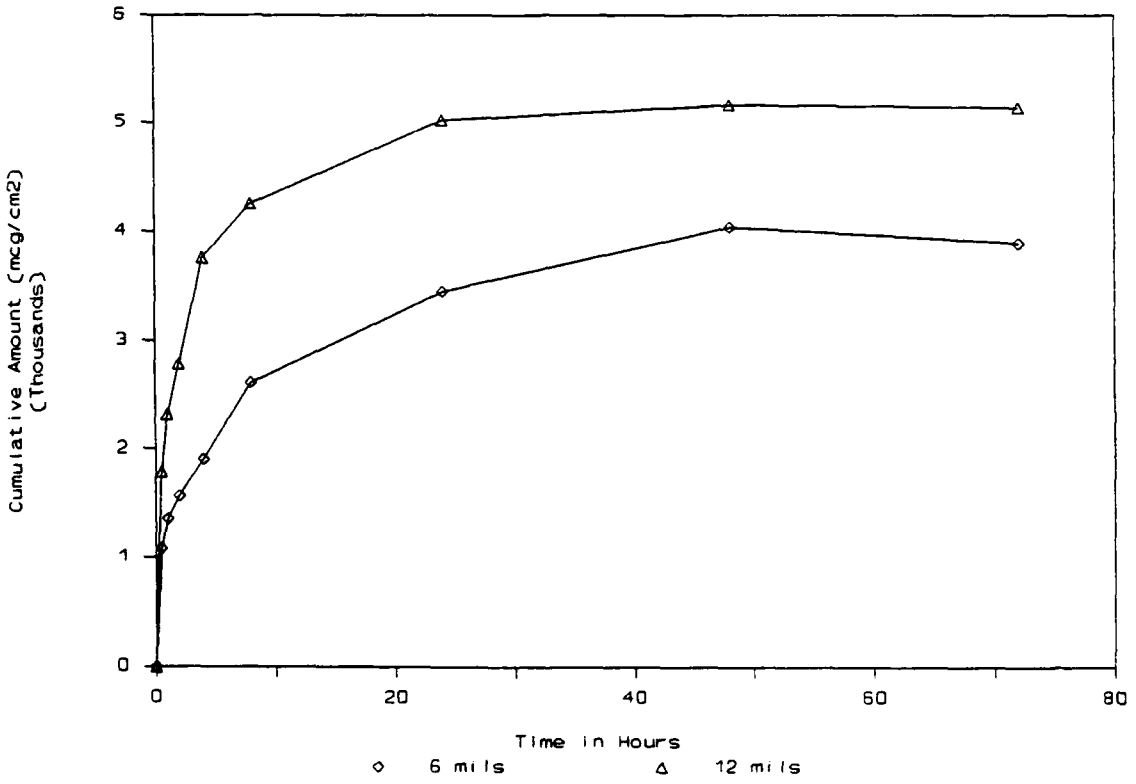


Figure 16. Drug Elution Profile of 30% Chlorhexidine Gluconate ADDs'- 6 and 12 mils thick: Formulation 2 and 5.

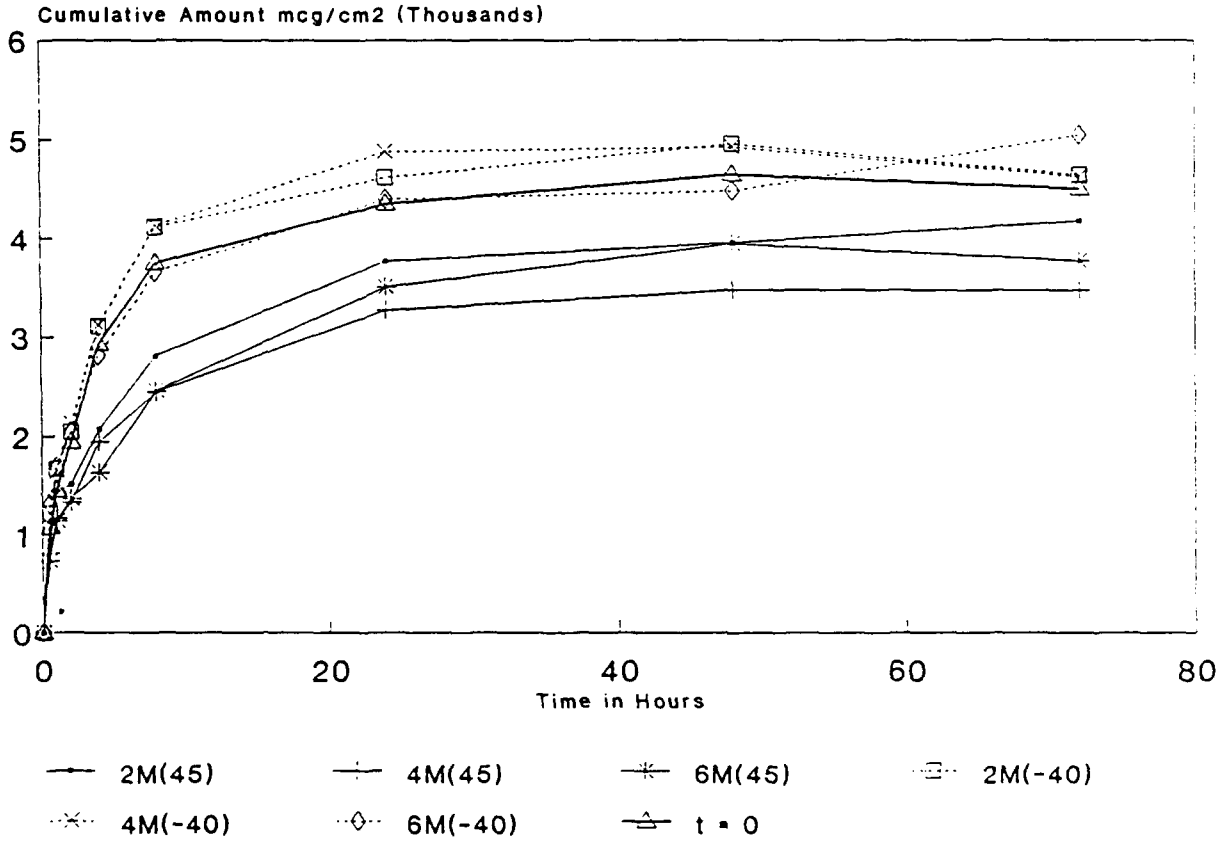
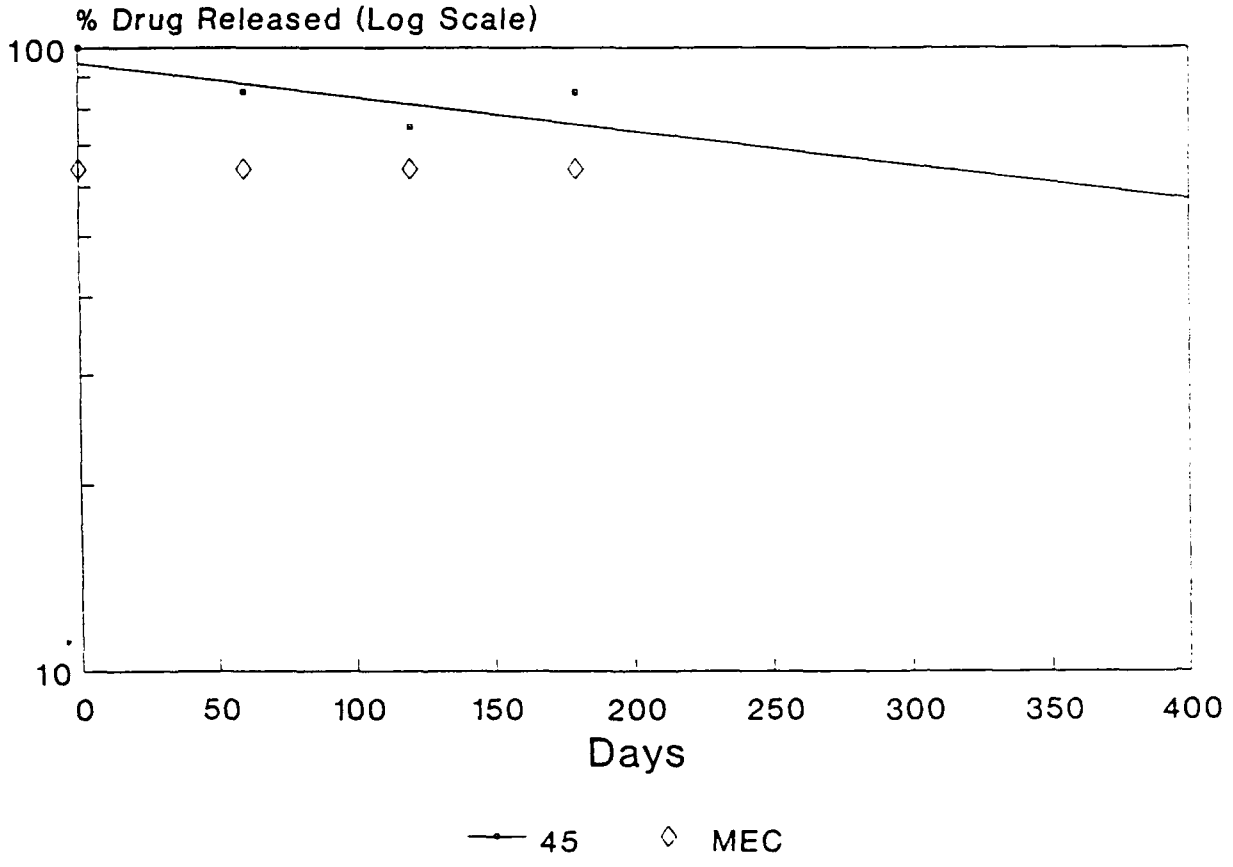
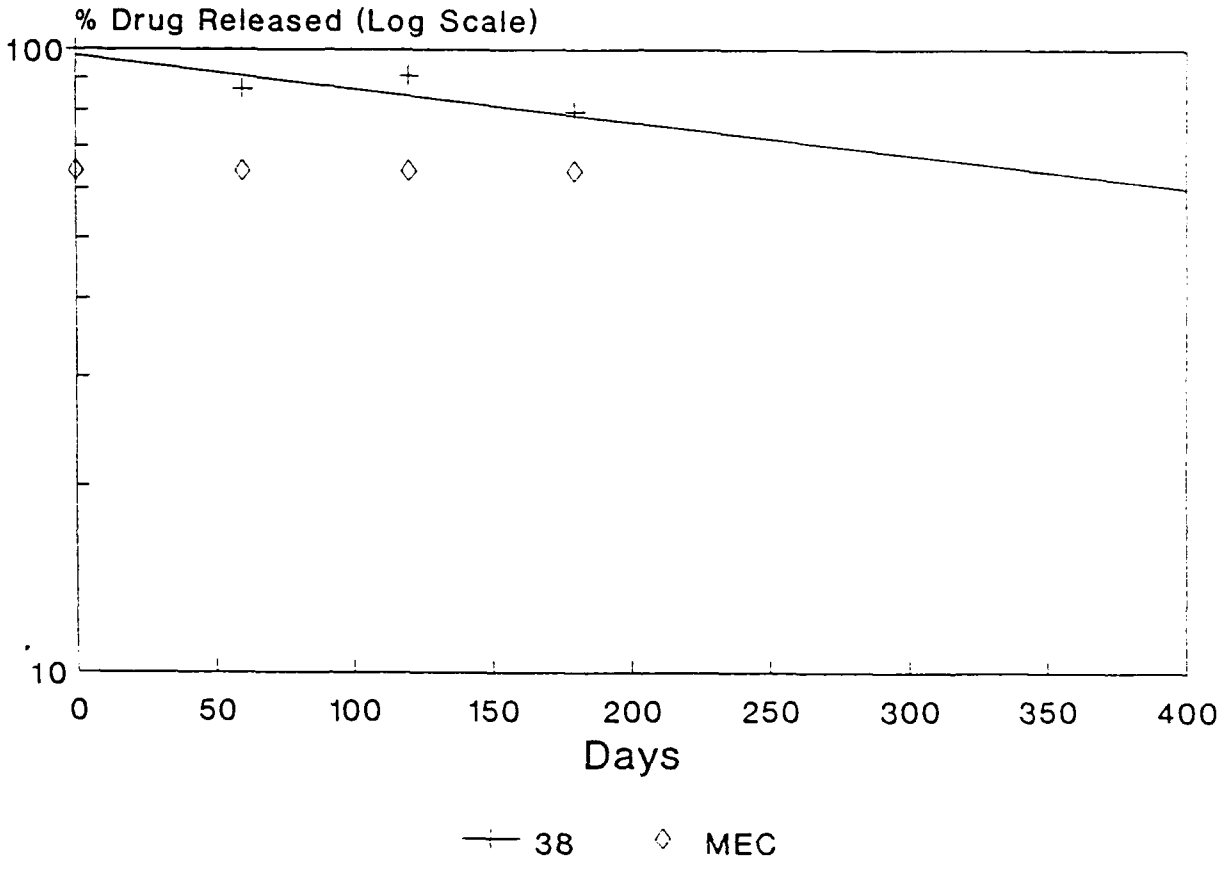


Figure 17. Elution Rates for the 30% Chlorhexidine Gluconate ADD's at t = 0 and Stored at the Temperature Extremes (-40^{0}C and 45^{0}C) for 2, 4 and 6 Months.



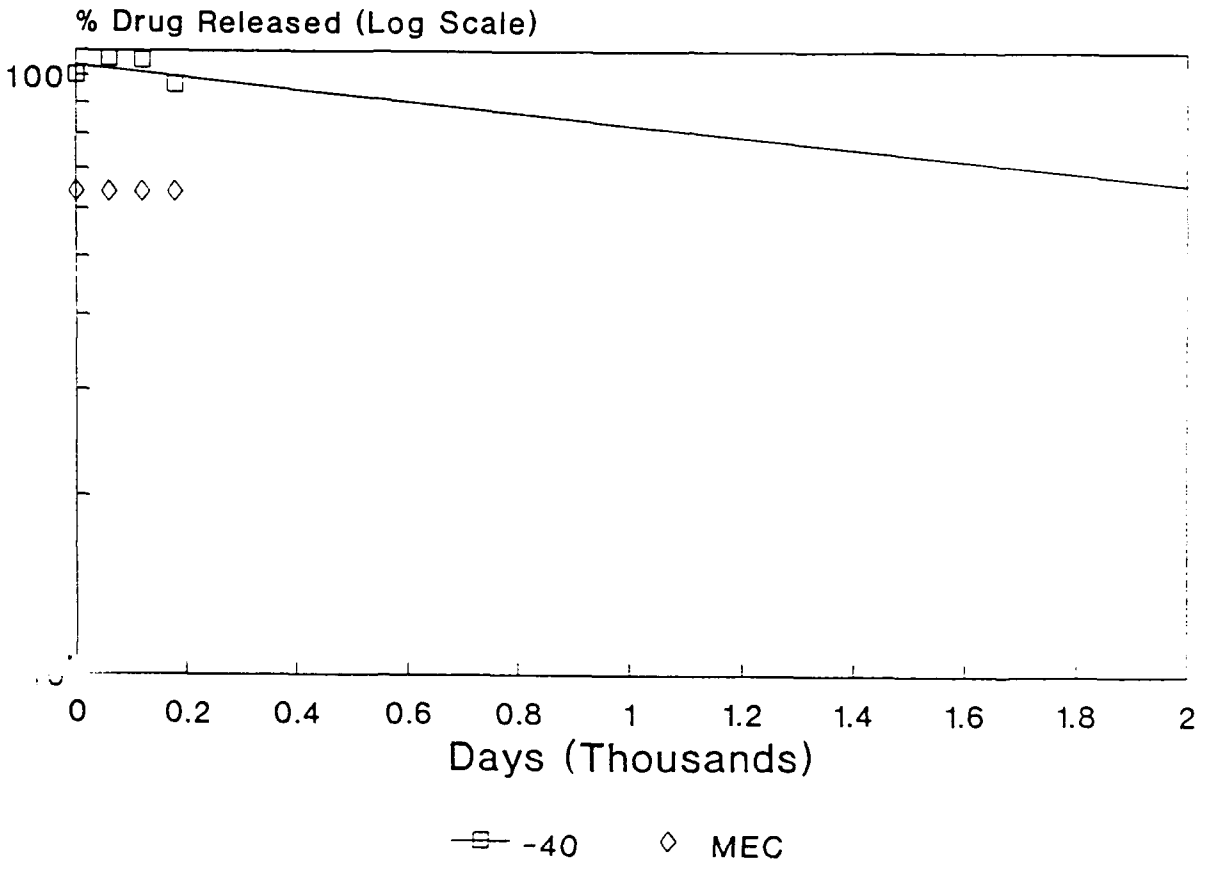
30/CHX

Figure 18. Shelf Stability Prediction for Chlorhexidine Gluconate ADDs'; Plot of Log Percent Drug Released Versus Time in Days for Samples Stored at 45°C.



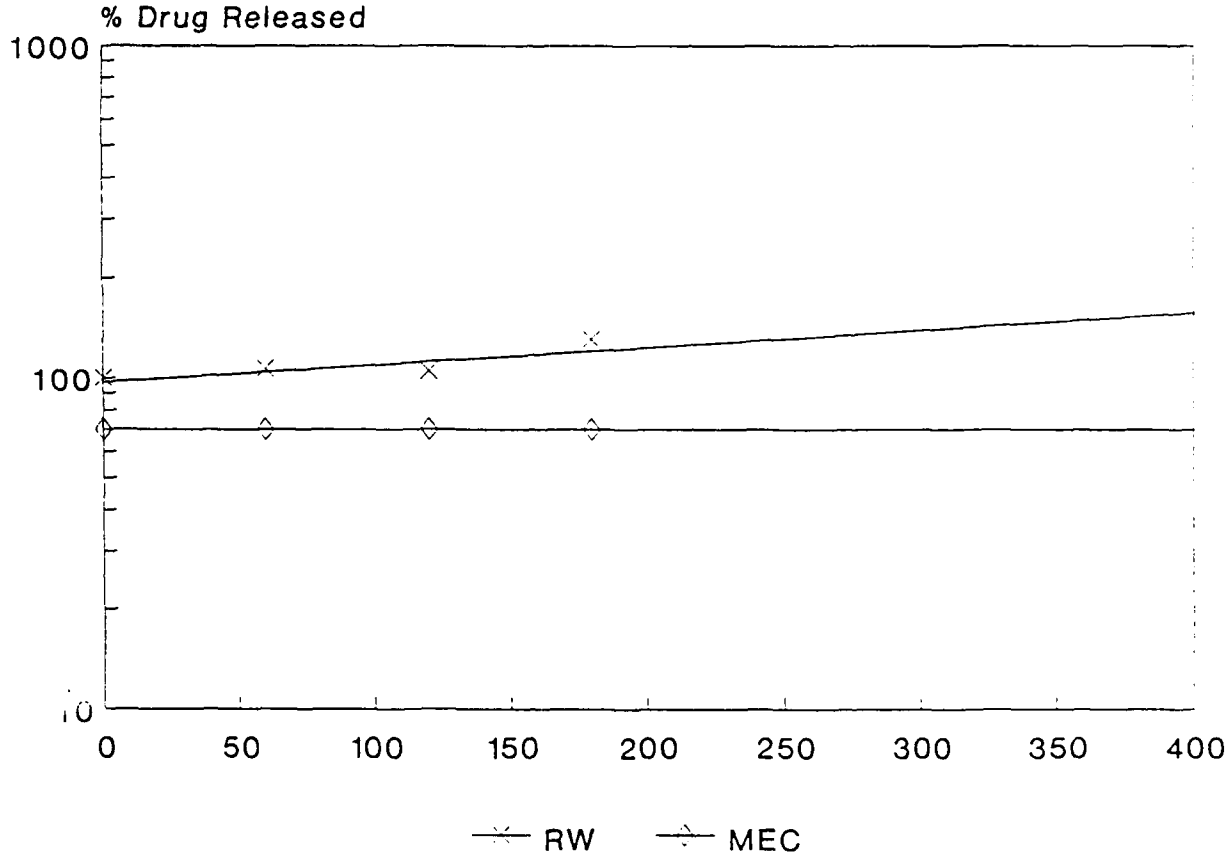
30/CHX

Figure 19. Shelf Stability Prediction for Chlorhexidine Gluconate ADDs'; Plot of Log Percent Drug Released Versus Time in Days for Samples Stored at 38°C.



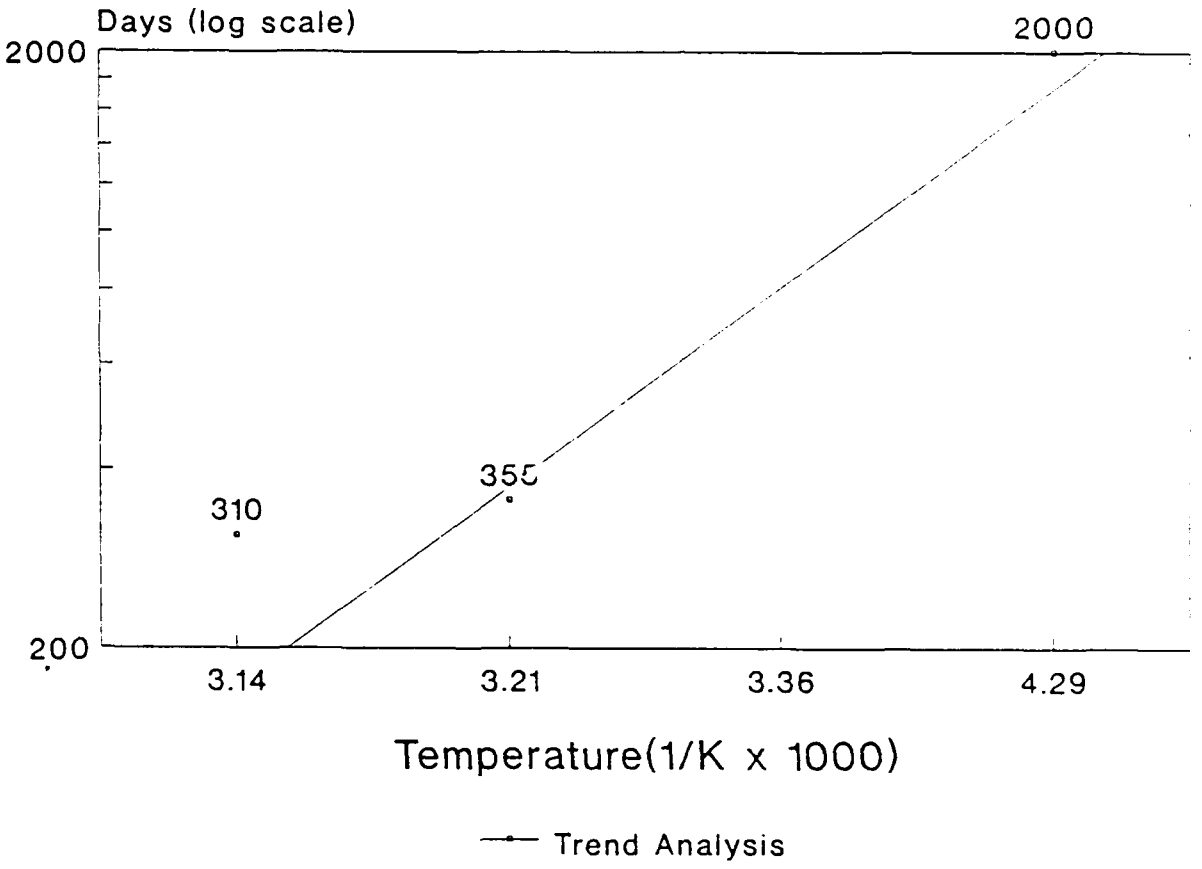
30/CHX

Figure 20. Shelf Stability Prediction for Chlorhexidine Gluconate ADDs'; Plot of Log Percent Drug Released Versus Time in Days for Samples Stored at -40°C.



30/CHX

Figure 21. Shelf Stability Prediction for Chlorhexidine Gluconate ADDs'; Plot of Log Percent Drug Released Versus Time in Days for Samples Stored at 23^{0}C Under Water.



30/CHX

Figure 22. Shelf Stability Prediction for Chlorhexidine Gluconate ADDs' Stored Under Normal Shelf Conditions.

The analysis of the elution samples for the 30% loaded chlorhexidine gluconate ADD's did not show any detectable amount of PCA. The same HPLC methodology was used to predict the shelf life of chlorhexidine gluconate in the dual loaded ADDs'. The dual loaded ADDs' incorporated only 10% of the lyophilized powder and HPLC analysis indicated these were also free of degradation products.

The physical examination of dual loaded ADDs' subjected to high temperatures showed a discoloration of the dressing. The chromatographic analysis of the eluates did not show any degradation products for chlorhexidine gluconate. Mixtures of the drug powders were subjected to the same temperature conditions and analyzed by HPLC. This analysis showed the concentrations of both drugs remained constant which indicates the absence of any interactive product.

The silver sulfadiazine elution curves for every condition showed an overall increase from the original value at t = 0. The increase in the concentration of silver sulfadiazine in the elution samples for the dual loaded ADDs' is attributable to its solubility in the L62 excipient. Elevated temperature increases the rate at which the drug reaches the saturation concentration. This is demonstrated by the increase in the elution rate of silver sulfadiazine stored at 38 and 45^{0}C (Figures 11, 13 and 15).

The ADD's subjected to the elevated temperatures turned dark brown in the island portion of the dressing. The in vitro microbiological zone of inhibition tests showed the efficacy of the dressings stored at elevated conditions. Also, literature states that the microbiological activity and efficacy of silver sulfadiazine is not compromised by strong color formation. Silver sulfadiazine in the solid state turns slightly yellow within one day upon exposure to light and remains in that state for at least two years. The extent of color formation increases with rise in temperature, but with no changes in silver and sulfadiazine content (12).

The graphical method used for predicting shelf life of chlorhexidine gluconate ADD's is dependant on the decrease in elution rates over time. This method is applicable for the elution rate of chlorhexidine gluconate in the dual loaded ADD's. However, the elution rate of silver sulfadiazine increases over time at elevated temperatures and the graphical prediction would show an infinite shelf life.

A dual loaded ADD incorporating 10% chlorhexidine gluconate should demonstrate an acceptable shelf life, since the 30% chlorhexidine gluconate ADD demonstrated a two year shelf life without any indication of degradation. This is verified by the elution data previously given where no appreciable decrease in the amount of drug eluted can be ascertained. The elution rate of

silver sulfadiazine from the dual ADD's increases with time, therefore, by definition these will have a satisfactory shelf life. The absence of any discernable interaction between the two drugs as determined by HPLC, also supports this. Finally, the in vitro zone of inhibition tests indicate these ADD's maintain efficacy after 6 months storage.

CONCLUSIONS

TCI has developed two prototype sustained release Antimicrobial Dermal Dressings. Both types of dressings incorporate antimicrobial agents to prevent infection up to 72 hours.

The first formulation, a 30% loaded chlorhexidine gluconate ADD, was formulated and tested successfully on guinea pigs. This dressing was effective in vivo against Strep. pyogenes, Staph. aureus and P. aeruginosa under prophylactic conditions. An exploratory accelerated stability study has demonstrated an effective two year shelf life for this product.

The second formulation, a dual loaded ADD incorporating 20% silver sulfadiazine and 10% chlorhexidine gluconate was also formulated and tested on guinea pigs. This dressing was effective against Staph. aureus and P. aeruginosa when used prophylactically. However, the effectiveness of this dressing against Candida is yet to be evaluated in vivo. These dressings were also subjected to exploratory shelf stability studies and demonstrated a two year shelf life for the product.

In conclusion, all tasks have been successfully completed. The prototype dressings have been shown to meet the design requirements of being easy to apply and effective against selected organisms.

RECOMMENDATIONS

The application for an Investigational New Drug (IND) for either of these two prototype dressings requires the statistical validation of the processes involved. This statistical validation was beyond the scope of this contract. All further work should address process validation.

The processing of the ADD's was dependent upon the quality of the lyophilized chlorhexidine gluconate powder (LCHX). There were occasions where the LCHX agglomerated during the dispersion stage of the process. Once the powder had agglomerated it could not be reworked even using elevated temperatures. Strategies to eliminate this problem should be defined.

Reaction rates double for every 10 degree increase in temperature. Both formulations of dressings have shown that storage at $-40^{0}C$ does not compromise their efficacy. It is recommended that future storage stability tests include an additional elevated temperature in order to give three data points above room temperature. This will facilitate predictions of shelf life under accelerated conditions.

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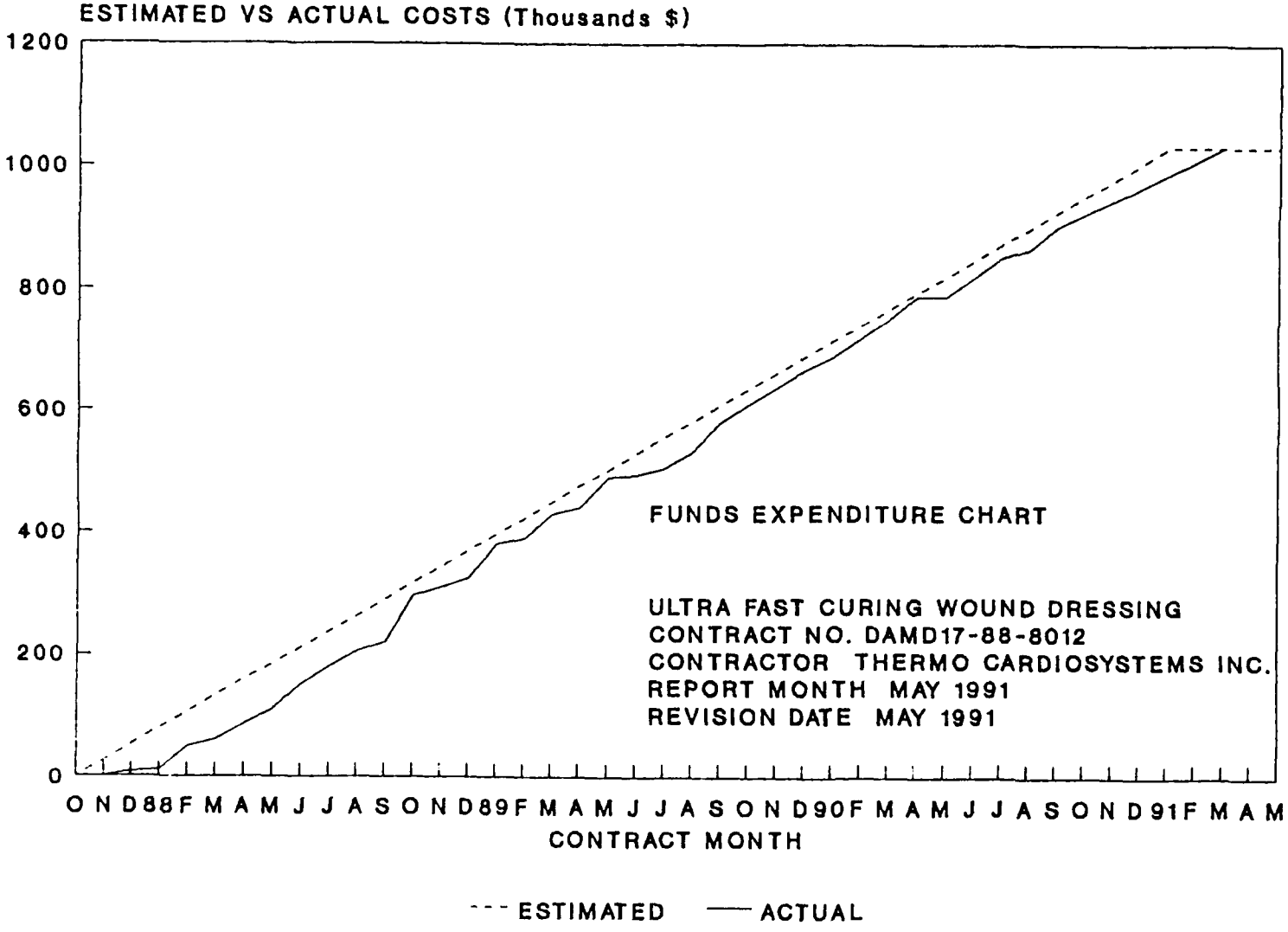

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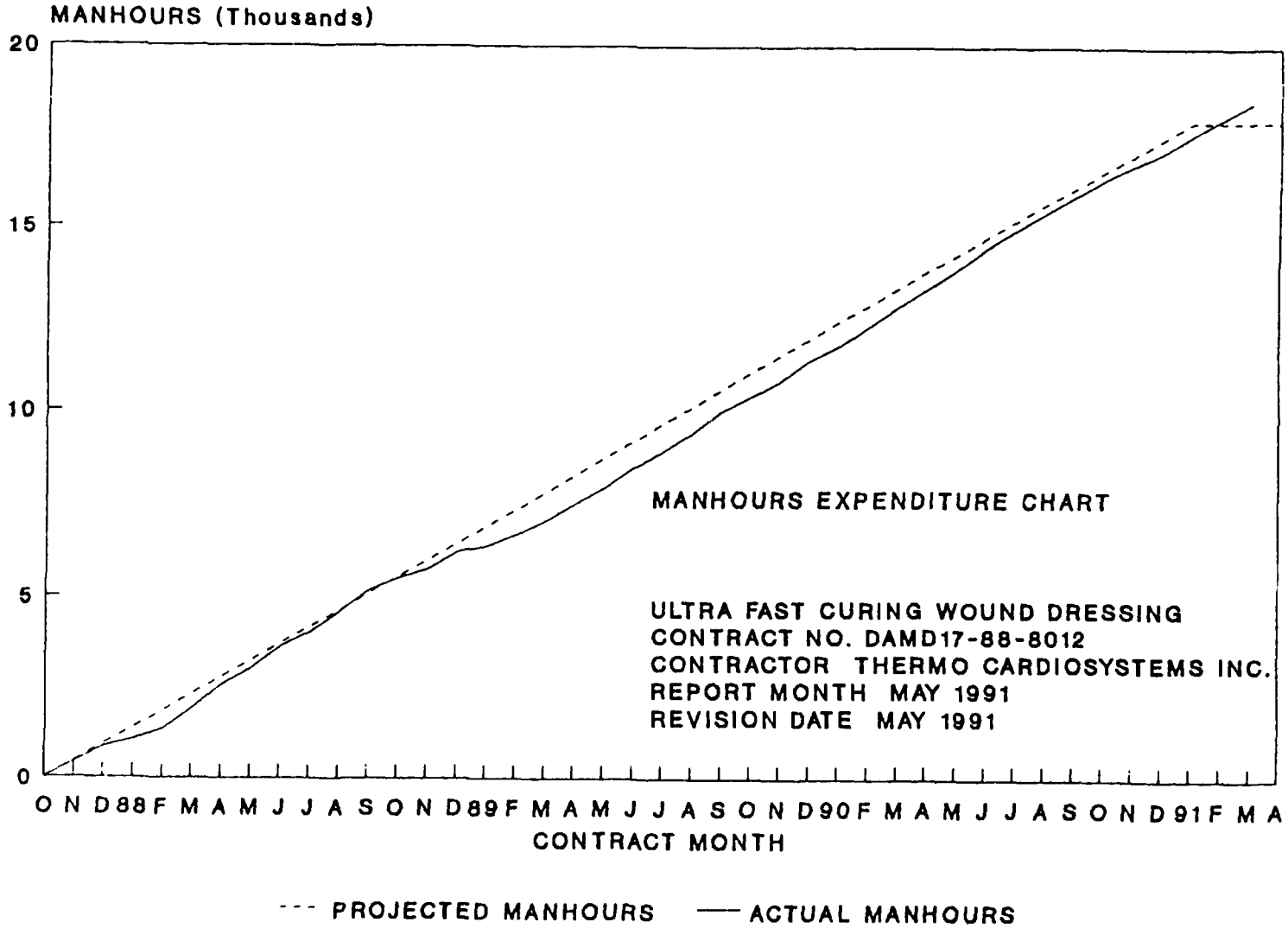

Attachment to Data Item A-5001B

Table I. Total Labor Hours for Contract Period

	Professional		Technical	
	Required	Used	Required	Used
	11638		6340	
Dasse		90		
Szycher		188		
Lobuglio		554		
Dempsey		5986		
Thirucote		5117		
Rolfe		296		
Williams		95		
Adams				4007
Gaffney				1528
Others				650
Total	11638	12326	6340	6185

APPENDIX I

CERTIFICATE OF ANALYSIS

Thermedics Inc.

CERTIFICATE OF ANALYSIS

Antimicrobial Dermal Dressings

Date	:	September 4, 1990.
30% Chlorhexidine Gluconate ADD's	:	Batch # 008031 PDDS1

Description	: A sterile 1.5 x 1.5 inch drug loaded island matrix; reinforced by a 2.5 x 2.5 inch adhesive backing, covered by a removable release liner and packaged in an aluminum pouch.
Color	: White to Off-white
Thickness	
total	: 0.611 mm $\pm$ 0.014 mm
perimeter	: 0.254 mm $\pm$ 0.013 mm.
Weight	
total	: 1.440 g $\pm$ 0.019 g.
Identification (I.R.)	: complies.
Dissolution time	: > 2.5 mg. per cm^2. in 24 hours
Biological Activity	: USP XXII, 1990
P. aeruginosa	positive.
S. aureus	positive.
Sterility (USP XXII, 1990)	: passes
Assay	: 135 mg. chlorhexidine gluconate/ADD.

Chemist 9/4/90

Manager 9/7/90

TCI
Thermo Cardiosystems Inc.
A subsidiary of Thermedics Inc. and Thermo Electron Corporation

CERTIFICATE OF ANALYSIS

Antimicrobial Dermal Dressings

Date: November 12, 1990

20% Silver sulfadiazine / 10% Chlorhexidine gluconate

Batch # 010181-PDDS2

Description	: A sterile 1.5 x 1.5 inch drug loaded island matrix; reinforced by a 2.5 x 2.5 inch adhesive backing, covered by a removable release liner and packaged in an aluminum pouch.
Color	: off white to cream colored
Thickness	
total	: 0.622 mm ± 0.014 mm
island	: 0.307 mm ± 0.014 mm
Weight	
total	: 1.475 ± 0.34 g
Identification (I.R.)	: complies
Dissolution time	
Silver sulfadiazine	: > 30 mcg per cm^2 in 24 hours
Chlorhexidine gluconate	: > 800 mcg per cm^2 in 24 hours
Biological activity	: USP XXII, 1990
P. aeruginosa	positive
S. aureus	positive
Sterility	: USP XXII, 1990 passes
Assay	:
Chlorhexidine gluconate	> 45 mg per patch

Chemist

Manager

470 Wildwood Street Post Office Box 2697 Woburn, MA 01888-2697 (617) 932-8068 Fax (617) 933-4470 Telex 755764

APPENDIX II

MICROBIOLOGICAL TEST RESULTS

toxikon

225 Wildwood Ave., Woburn, MA 01801
Telephone: (617) 933-6903
Fax: (617) 933-9196

TEST RESULT CERTIFICATE

Client: Thermedics, Inc.

Address: 470 Wildwood Avenue
P.O. Box 2999
Woburn, MA 01888-1799

Project #: 90-1835

Date of Test: 08/28/90
Test Completion: 09/04/90

P.O. #: 24156-897

Contact: R. Thirucote

TEST ARTICLE DESCRIPTION: Chlorhexidine Gluconate Dressing

Lot# N/A [008031-PDDS1] t=0

NAME OF STUDY: Membrane Filtration Sterility

REFERENCE: USP XXII, 1990, Pp. 1483-1488.

GENERAL PROCEDURE: The test articles (2 units) were aseptically pooled with 300 ml of Fluid D. The extract was then decanted into a sterile container and filtered though a sterile membrane filter. The membrane was then removed from the filter holder and cut in half. One half was immersed in 100 ml of Fluid Thioglycollate Medium (FTM) and one half was immersed in 100 ml of Trypticase Soy Broth (TSB). Each vessel was incubated at 30-35°C and 20-25°C respectively. The contents of each vessel were examined for growth during the 7 day incubation period.

RESULTS: There was no growth observed in either media inoculated with the test article during the 7 day observation period.

CONCLUSION: The test article is considered sterile according to the procedures outlined in USP XXII via membrane filtration technique.

AUTHORIZED PERSONNEL:

Steven P. Lynn, Ph.D
Study Director

Susan Yadlon, B.S.
Quality Assurance

toxikon

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Telephone: (617) 933-6903
Fax: (617) 933-9196

TEST RESULT CERTIFICATE

Client: Thermedics, Inc.

Address: 470 Wildwood Street
P.O. Box 2999
Woburn, MA 01801

Project #: 90-1836

Date of Test: 08/23/90
Test Completion: 08/27/90
P.O. #: 24139-897

Contact: R. Thirucote

TEST ARTICLE DESCRIPTION: Chlorhexidine Gluconate Dressing

LOT #: N/A [008031-PDDS1] t=0

NAME OF STUDY: Zone of Inhibition

REFERENCE: Based on the method described in USP XXII, 1990.

GENERAL PROCEDURE: The test article was analyzed for its ability to produce a zone of inhibition against cultures of *Staphylococcus aureus* (*S. aureus*) and *Pseudomonas aeruginosa* (*P. aeruginosa*). The test article (three 0.8 cm diameter discs) and placebo discs (three 0.8 cm diameter discs) were placed on the surface of Trypticase Soy Agar containing the test organism. The positive control for *S. aureus* was a mixture of penicillin and streptomycin. The positive control for *P. aeruginosa* was ampicillin. The negative control for both organisms was an untreated filter disc. Three plates were used for each determination. The plates were inverted and incubated at 30-35°C for 72 hours.

RESULTS:

	Zone of Inhibition (in cm)							
	S. aureus				*P. aeruginosa*			
	1	2	3	Ave	1	2	3	Ave
Neg. Control	0	0	0	0	0	0	0	0
Pos. Control	1.40	1.30	1.30	1.33	2.0	2.0	2.0	2.0
Test Article	1.50	1.80	1.70	1.67	1.50	1.60	1.50	1.53

CONCLUSION: The test article does possess antimicrobial activity against *S. aureus* and *P. aeruginosa*. The size of the zone of inhibition is indicative of antimicrobial activity, but is not a quantitative evaluation of potency as outlined in this study.

AUTHORIZED PERSONNEL:

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TEST RESULT CERTIFICATE

Client: Thermo Cardiosystems, Inc.

Address: P.O. Box 2697
470 Wildwood Avenue
Woburn, MA 01801

Project #: 91-0503

Date of Test: 03/13/91
Test Completion: 03/20/91

P.O. #: 3829-897

Contact: R. Thirucote

TEST ARTICLE DESCRIPTION: Chlorhexidine Gluconate Add's

B.N.: 008031-PDDS1 t=6M

NAME OF STUDY: Membrane Filtration Sterility

REFERENCE: USP XXII, 1990, Pp. 1483-1488.

GENERAL PROCEDURE: The test articles (2 units) were aseptically pooled with 300 ml of Fluid D. The extract was then decanted into a sterile container and filtered though a sterile membrane filter. The membrane was then removed from the filter holder and cut in half. One half was immersed in 100 ml of Fluid Thioglycollate Medium (FTM) and one half was immersed in 100 ml of Trypticase Soy Broth (TSB). Each vessel was incubated at 30-35°C and 20-25°C respectively, for seven days. The contents of each vessel were examined daily for growth.

RESULTS: There was no growth observed in either media for the test article.

CONCLUSION: The test article is considered sterile according to the procedures outlined in USP XXII via membrane filtration technique.

AUTHORIZED PERSONNEL:

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Study Director

Susan Yadlon, B.S.
Quality Assurance

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TEST RESULT CERTIFICATE

Client: Thermo Cardiosystems, Inc.
Address: 470 Wildwood Avenue
P.O. Box 2697
Woburn, MA 01888
Project #: 91-0504

Date of Test: 03/15/91
Test Completion: 03/18/91
P.O. #: 3829-897
Contact: R. Thirucote

TEST ARTICLE DESCRIPTION: Chlorhexidine Gluconate Add's 30%

B.N #: 008031-PDDS1 t=6M

NAME OF STUDY: Zone of Inhibition

REFERENCE: Based on the method described in USP XXII, 1990.

GENERAL PROCEDURE: The test article was analyzed for its ability to produce a zone of inhibition against cultures of *Staphylococcus aureus* (*S. aureus*) and *Pseudomonas aeruginosa* (*P. aeruginosa*). The test article (three 0.8 cm diameter discs) and placebo discs (three 0.8 cm diameter discs) were placed on the surface of Trypticase Soy Agar (TSA) and Potatoe Dextrose Agar (PDA) containing the test organism. The positive control for *S. aureus* was a mixture of penicillin and streptomycin. The positive control for *P. aeruginosa* was ampicillin. The negative control for both organisms was an untreated filter disc. Three plates were used for each determination. The plates were inverted and incubated at 30-35°C for 72 hours.

RESULTS:

Zone of Inhibition (in mm)

	S. aureus (TSA)				*P. aeruginosa* (PDA)			
	1	2	3	Ave	1	2	3	Ave
Neg. Control	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Pos. Control	4.5	3.7	3.7	4.0	3.8	4.1	4.0	4.0
Test Article	2.8	2.8	2.4	2.7	2.5	2.5	2.4	2.5

CONCLUSION: The test article does possess antimicrobial activity against *S. aureus* and *P. aeruginosa*. The size of the zone of inhibition is indicative of antimicrobial activity, but is not a quantitative evaluation of potency as outlined in this study.

AUTHORIZED PERSONNEL:

Laxman S. Desai, D.Sc.
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TEST RESULT CERTIFICATE

Client: Thermedics, Inc.

Address: 470 Wildwood Avenue
P.O. Box 2999
Woburn, MA 01888-1799

Project #: 90-2152.1

Date of Test: 11/21/90
Test Completion: 11/28/90

P.O. #: 24801-897

Contact: R. Thirucote

TEST ARTICLE DESCRIPTION: Combination Silver Sulfadiazine/ Chlorhexidine Gluconate Dressing

Lot#: 010181-PDDS2 t=0

NAME OF STUDY: Membrane Filtration Sterility

REFERENCE: USP XXII, 1990, Pp. 1483-1488.

GENERAL PROCEDURE: The test articles (2 units) were aseptically pooled with 300 ml of Fluid D. The extract was then decanted into a sterile container and filtered though a sterile membrane filter. The membrane was then removed from the filter holder and cut in half. One half was immersed in 100 ml of Fluid Thioglycollate Medium (FTM) and one half was immersed in 100 ml of Trypticase Soy Broth (TSB). Each vessel was incubated at 30-35°C and 20-25°C respectively. The contents of each vessel were examined for growth during the 7 day incubation period.

RESULTS: There was no growth observed in either media inoculated with the test article during the 7 day observation period.

CONCLUSION: The test article is considered sterile according to the procedures outlined in USP XXII via membrane filtration technique.

AUTHORIZED PERSONNEL:

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TEST RESULT CERTIFICATE

Client: Thermedics, Inc.

Address: 470 Wildwood Street
P.O. Box 2999
Woburn, MA 01888

Project #: 90-2153

Date of Test: 11/26/90
Test Completion: 11/30/90
P.O. #: 24802-897

Contact: R. Thirucote

TEST ARTICLE DESCRIPTION: Combination Silver Sulfadiazine/ Chlorhexidine Gluconate Dressing

LOT #: B.N. 010181-PDDS2 t=0

NAME OF STUDY: Zone of Inhibition

REFERENCE: Based on the method described in USP XXII, 1990.

GENERAL PROCEDURE: The test article was analyzed for its ability to produce a zone of inhibition against cultures of *Staphylococcus aureus* (*S. aureus*) and *Pseudomonas aeruginosa* (*P. aeruginosa*). The test article (three 0.8 cm diameter discs) and placebo discs (three 0.8 cm diameter discs) were placed on the surface of Trypticase Soy Agar containing the test organism. The positive control for *S. aureus* was a mixture of penicillin and streptomycin. The positive control for *P. aeruginosa* was ampicillin. The negative control for both organisms was an untreated filter disc. Three plates were used for each determination. The plates were inverted and incubated at 30-35°C for 72 hours.

RESULTS:

	Zone of Inhibition (in cm)							
	S. aureus				*P. aeruginosa*			
	1	2	3	Ave	1	2	3	Ave
Neg. Control	0	0	0	0	0	0	0	0
Pos. Control	1.2	1.1	1.8	1.37	1.9	1.8	2.0	1.9
Test Article	1.6	1.4	1.7	1.57	1.4	1.5	1.6	1.5

CONCLUSION: The test article does possess antimicrobial activity against *S. aureus* and *P. aeruginosa*. The size of the zone of inhibition is indicative of antimicrobial activity, but is not a quantitative evaluation of potency as outlined in this study.

AUTHORIZED PERSONNEL:

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Study Director

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Quality Assurance

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TEST RESULT CERTIFICATE

Client: Thermo Cardiosystems, Inc.
Address: 470 Wildwood Avenue
P.O. Box 2697
Woburn, MA 01888
Contact: R. Thirucote

Technical Initiation: 05/23/91
Technical Completion: 05/30/91
Final Report: 05/30/91
P.O. #: 4120-897

Project #: 91-0788

TEST ARTICLE: 20% Silver Sulfadiazine 10% Chlorhexidine Gluconate ADDs'

Lot#: B.N 010181-PDDS2 t=6M

NAME OF STUDY: Membrane Filtration Sterility
REFERENCE: USP XXII, 1990

GENERAL PROCEDURE: The test articles (2 units) were aseptically pooled with 300 ml of Fluid D, decanted, and filtered though a sterile membrane filter. The membrane was removed from the filter holder and cut in half. One half was immersed in 100 ml of Fluid Thioglycollate Medium (FTM) and the other half immersed in 100 ml of Trypticase Soy Broth (TSB). Each vessel was incubated for 7 days at 30-35°C and 20-25°C, respectively. The contents of each vessel were examined for growth. One spore strip (positive control) was tested in 30 ml of TSB at 50-55°C.

RESULTS: There was no growth observed in either media for the test article. The positive control spore strip exhibited growth within 24 hours of incubation.

CONCLUSION: The test article is considered sterile according to the procedures outlined in USP XXII via membrane filtration technique.

AUTHORIZED PERSONNEL:

Laxman S. Desai, D.Sc.
Study Director

Susan Yadlon, B.S.
Quality Assurance

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Date of Test: 05/29/91
Test Completion: 05/30/91
Report Date: 06/03/91
P.O. #: 4120-897

Project #: 91-0787

Contact: R. Thirucote

TEST ARTICLE DESCRIPTION: 20% Silver Sulfadiazine
10% Chlorhexidine Gluconate Add's

Lot #: B.N. 010181-PDDS2 t=6M

NAME OF STUDY: Zone of Inhibition

REFERENCE: Based on the method described in USP XXII, 1990.

GENERAL PROCEDURE: The test article was analyzed for its ability to produce a zone of inhibition against cultures of *Staphylococcus aureus* (*S. aureus*) and *Pseudomonas aeruginosa* (*P. aeruginosa*). The test article, cut into 0.8 cm diameter discs was placed on the surface of Medium 19 Agar containing the test organisms. The positive control was a mixture of penicillin and streptomycin. The negative control (placebo) was supplied by the Sponsor. Three plates were used for each determination. The plates were inverted and incubated at 30-35°C for 24 hours.

RESULTS:

Zone of Inhibition (in mm)

	S. aureus				*P. aeruginosa*			
	1	2	3	Ave	1	2	3	Ave
Neg. Control	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Pos. Control	3.5	2.5	4.0	3.3	3.0	5.0	2.0	3.3
Test Article								
RT	2.5	2.5	2.0	2.3	1.5	2.0	1.5	1.7
23°/H_2O	2.0	1.5	2.0	1.8	1.5	2.0	2.5	2.0
38°/90% RH	2.0	2.0	2.5	2.2	3.5	1.5	1.5	2.2
-40°	3.0	2.0	2.0	2.3	2.5	1.5	2.0	2.0
45°/90% RH	1.0	3.0	1.5	1.8	2.0	2.0	1.0	1.7

CONCLUSION: The test article does possess antimicrobial activity against *S. aureus* and *P. aeruginosa*. The size of the zone of inhibition is indicative of antimicrobial activity, but is not a quantitative evaluation of potency as outlined in this study.

AUTHORIZED PERSONNEL:

Laxman S. Desai, D.Sc.
Study Director

Susan Yadlon, B.S.
Quality Assurance

APPENDIX III

IN VITRO DATA SHEETS

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031E-PDDS1 (Set 1)

STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	628592	586368	607480
500	2907409	2872586	2889998
800	4823876	4834027	4828952
1000	6348941	6321570	6335256
2000	13401626	12688172	13044899

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	434.5	434.5	1229.7	1229.7
1	528.0	538.9	1525.1	295.3
2	740.8	754.0	2133.8	608.7
4	1143.6	1162.1	3288.9	1155.1
8	1418.7	1447.3	4095.9	807.0
24	1562.4	1597.9	4521.9	426.0
48	1749.1	1788.1	5060.4	538.5
72	1652.4	1696.1	4800.0	-260.5

Regression Output:

Constant	-176096.
Std Err of Y Est	200957.1
R Squared	0.998588
No. of Observations	6
Degrees of Freedom	4
X Coefficient(s)	6537.082
Std Err of Coef.	122.3070

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	2977017	2603097	2413290	2664468	234196.2
1	3493647	3103185	3230110	3275647.	162625.0
2	4959537	4219846	4820048	4666477	320908.8
4	7994378	6431314	7474029	7299907	649887.7
8	9772500	8217787	9304384	9098223.	651234.5
24	10647790	8783515	10680735	10037346	886694.8
48	11437887	10949407	11386142	11257812	219096.0
72	10966207	9232918	11677629	10625584	1026700.

Formulation	Wt.%		Date: 08/23/90
Chlorhexidine	30	"After E-Beam sterilization"	File: B008031E
Propylene Glycol	6	Set 1	
PEG 300	24		
Matrix	40		

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031E-PDDS1 Set 2

STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	512785	518900	515843
500	2898234	2867061	2882648
800	4991913	4998578	4995246
1000	5603535	5656796	5630166
2000	12071584	12878013	12474799

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	319.6	319.6	904.4	904.4
1	472.4	480.4	1359.5	455.0
2	601.7	613.5	1736.2	376.8
4	889.3	904.3	2559.3	823.1
8	1176.8	1199.1	3393.4	834.1
24	1446.8	1476.2	4177.6	784.2
48	1459.9	1496.0	4233.8	56.2
72	1448.2	1484.7	4201.6	-32.2

Regression Output:

Constant	-147175.
Std Err of Y Est	267615.0
R Squared	0.997240
No. of Observations	6
Degrees of Freedom	4

X Coefficient(s) 6223.124
Std Err of Coef. 163.6756

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	1927035	2027821	1876734	1887554	1489223		1841673.	184115.7
1	3541438		2557354		2278756		2792516	541643.9
2	4585628		3276397		2929749		3597258	713067.3
4	6519381		5354612		4287108		5387033.	911609.9
8	8056236		6956756		6516252		7176414.	647598.1
24	9508963		8772552		8286903		8856139.	502392.8
48	9385385		8640956		8786748		8937696.	322110.4
72	9169720		8651421		8773646		8864929	221220.7

Formulation	Wt.%		
Chlorhexidine	30	"After E-Beam sterilization"	Date: 08/27/90
Propylene Glycol	6	Set 2	File: E0080312.WK1
PEG 300	24		
Matrix	40		

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031-PDDS1 2 Month Sample @ 45 C/ 90% RH

STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	467687	448195	457941
500	3040010	2886689	2963350
800	4782207	4784922	4783565
1000	5675335	5459266	5567301
2000	12726955	12585654	12656305

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	334.0	334.0	945.2	945.2
1	496.0	504.4	1427.3	482.2
2	520.1	532.5	1506.9	79.6
4	717.3	730.3	2066.8	559.9
8	974.5	992.4	2808.5	741.7
24	1305.9	1330.3	3764.7	956.2
48	1364.7	1397.4	3954.6	189.9
72	1440.4	1474.5	4172.8	218.2

Regression Output:

Constant	-218372.	2 MONTH STABILITY
Std Err of Y Est	313113.3	45 C/90% RH
R Squared	0.996322	
No. of Observations	6	
Degrees of Freedom	4	

X Coefficient(s) 6304.249
Std Err of Coef. 191.5027

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	1776137	1767078	1752691	1655524	2206288	2164971	1887114.	215059.8
1	2501919		2605821		3618084		2908608	503465.3
2	2601741		3002645		3576465		3060283.	400011.1
4	3260297		4336471		5314697		4303821.	839022.9
8	5348750		5605877		6820239		5924955.	641705.1
24	7974299		7664704		8404695		8014566	303438.8
48	8425247		7619909		9110626		8385260.	609239.1
72	8438032		7722994		10425168		8862064.	1143179.

Formulation	Wt.%
Chlorhexidine	30
Propylene Glycol	6
PEG 300	24
Matrix	40

Date: 10/29/90
File: 2MSTA-45

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031-PDDS1 2 Month Sample @ 38 C/90% RH

STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	626401	622783	624592
500	3037933	3021214	3029574
800	5340031	5204862	5272447
1000	6333264	6046154	6189709
2000	11743334	11517463	11630399

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	303.2	303.2	858.0	858.0
1	453.1	460.7	1303.8	445.8
2	583.1	594.5	1682.3	378.5
4	879.3	893.8	2529.6	847.3
8	1172.3	1194.3	3379.9	850.3
24	1397.1	1426.4	4036.7	656.9
48	1386.0	1420.9	4021.3	-15.4
72	1398.4	1433.1	4055.7	34.4

Regression Output:

Constant	169858.1	2 MONTH STABILITY
Std Err of Y Est	280538.4	38 C/90% RH
R Squared	0.996567	
No. of Observations	6	
Degrees of Freedom	4	
X Coefficient(s)	5847.175	
Std Err of Coef.	171.5796	

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	2125830	2117694	1848705	1728560	1911143	1923725	1942609.	141542.8
1	2620294		3031225		2806785		2819434.	168000.1
2	3363007		3721117		3654393		3579505.	155492.2
4	4953856		5162431		5816949		5311078.	367699.5
8	6677589		6931111		7465099		7024599.	328225.6
24	8017622		8383899		8615243		8338921.	246041.9
48	8108139		8615774		8098531		8274148	241597.9
72	8296233		8274380		8462823		8346812	87438.23

Formulation	Wt.%
Chlorhexidine	30
Propylene Glycol	6
PEG 300	24
Matrix	40

Date: 10/31/90
File: 2MSTA-38.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031-PDDS1 2 Month Sample @ RT

STANDARD CALIBRATION CURVE

= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
500	3226522	3096717	3161620
800	5019617	5236543	5128080
1000	6157377	6295124	6226251
2000	12265064	12565648	12415356

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	377.6	377.6	1068.6	1068.6
1	537.0	546.5	1546.5	477.9
2	617.4	630.8	1785.3	238.8
4	924.8	940.3	2661.0	875.7
8	1292.7	1315.8	3723.7	1062.7
24	1606.9	1639.2	4638.9	915.2
48	1671.0	1711.2	4842.6	203.7
72	1699.7	1741.5	4928.4	85.8

Regression Output:

Constant	58610.99	2 MONTH STABILITY
Std Err of Y Est	77878.70	ROOM TEMPERATURE
R Squared	0.999783	
No. of Observations	5	
Degrees of Freedom	3	
X Coefficient(s)	6194.942	
Std Err of Coef.	52.60153	

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	2279151	2276466	2357840	2254422	2663956	2554740	2397762.	156217.1
1	3026535		3761713		3368010		3385419.	300387.5
2	3594926		4425371		3630063		3883453.	383462.0
4	5079486		6632755		5651642		5787961	641403.8
8	7827790		9056229		7315886		8066635	730289.2
24	10302011		10737379		8999629		10013006	738280.2
48	9549833		10528555		11152494		10410294	659605.8
72	12435010		10346774		8982704		10588162	1419696.

Formulation	Wt.%
Chlorhexidine	30
Propylene Glycol	6
PEG 300	24
Matrix	40

Date: 11/1/90
File: 2MSTA-RT.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031-PDDS1 2 Month Sample @ RT Under Water

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STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	626401	622783	624592
500	3037933	3021214	3029574
800	5340031	5204862	5272447
1000	6333264	6046154	6189709
2000	11743334	11517463	11630399

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	414.5	414.5	1173.0	1173.0
1	529.7	540.1	1528.5	355.5
2	676.0	689.2	1950.5	422.0
4	1053.2	1070.1	3028.3	1077.7
8	1434.4	1460.8	4133.9	1105.6
24	1668.4	1704.3	4823.1	689.2
48	1704.0	1745.7	4940.4	117.3
72	1729.1	1771.7	5013.9	73.5

Regression Output:

Constant	169858.1	2 MONTH STABILITY
Std Err of Y Est	280538.4	23 C UNDER WATER
R Squared	0.996567	
No. of Observations	6	
Degrees of Freedom	4	
X Coefficient(s)	5847.175	
Std Err of Coef.	171.5796	

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	2424855	2323061	3118498	3246501	2276340	2171426	2593530.	424662.9
1	3080080		3597024		3125047		3267383.	233812.7
2	3994260		4393172		3980116		4122516	191469.7
4	6684914		5969763		6328969		6327882	291960.1
8	9068202		8059535		8543785		8557174	411895.3
24	10040597		9885297		9850336		9925410	32690.59
48	10597998		9603919		10198670		10133529	408436.6
72	10488406		10328725		10023552		10280227	192849.3

Formulation	Wt.%
Chlorhexidine	30
Propylene Glycol	6
PEG 300	24
Matrix	40

Date: 10/31/90
File: 2MSTA-RW.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031-PDDS1 2 Month Sample @ -40 C

STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0		0
100	626401	622783	624592
500	3037933	3021214	3029574
800	5340031	5204862	5272447
1000	6333264	6046154	6189709
2000	11974791	12439009	12206900

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	429.8	429.8	1216.3	1216.3
1	579.5	590.3	1670.5	454.3
2	705.4	719.9	2037.3	366.8
4	1079.2	1096.8	3104.1	1066.7
8	1425.4	1452.4	4110.2	1006.1
24	1595.5	1631.1	4616.1	505.9
48	1711.7	1751.6	4957.0	340.9
72	1597.5	1640.3	4642.1	-314.9

Regression Output:

Constant	65627.83
Std Err of Y Est	175155.4
R Squared	0.998776
No. of Observations	6
Degrees of Freedom	4
X Coefficient(s)	6120.330
Std Err of Coef.	107.1265

2 MONTH STABILITY
-40 C

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	3005261	3001797	2907659	2908428	2188405	2164476	2696004.	369515.4
1	3747506		3869550		3220932		3612662.	281440.7
2	4208834		4393063		4546986		4382961	138234.6
4	7330400		6343106		6338632		6670712.	466472.9
8	8921695		9107754		8338855		8789434.	327537.2
24	10259998		9456351		9775574		9830641	330390.0
48	11104808		9901390		10619253		10541817	494335.2
72	10357488		9353494		9817888		9842956.	410261.9

Formulation	Wt.%
Chlorhexidine	30
Propylene Glycol	6
PEG 300	24
Matrix	40

Date: 10/30/30
File: 2MSTA-40.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031-PDDS1 4 Month Sample @ 45 C/ 90% RH

STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	483774	496960	490367
500	3175808	3019575	3097692
800	4972109	5073741	5022925
1000	6270407	6372312	6321360
2000	12105367	11985874	12045621

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	286.1	286.1	809.7	809.7
1	403.3	410.5	1161.6	352.0
2	457.9	468.0	1324.4	162.8
4	674.8	686.2	1942.0	617.6
8	846.6	863.4	2443.6	501.6
24	1135.2	1156.4	3272.5	828.9
48	1199.1	1227.5	3473.7	201.2
72	1195.3	1225.3	3467.6	-6.1

Regression Output:

Constant	40097.48	4 MONTH STABILITY
Std Err of Y Est	162188.6	45 C/90% RH
R Squared	0.998935	
No. of Observations	6	
Degrees of Freedom	4	

X Coefficient(s) 6076.676
Std Err of Coef. 99.19593

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	1659118	1640331	2160768	2034666	1582085	1594680	1778608	230022.1
1	2322659		2829765		2320176		2490866.	239639.4
2	2553272		3137565		2777239		2822692	240692.1
4	3826457		4452011		4342995		4140487.	386189.1
8	4342395		4975944		6234537		5184492	786173.0
24	5947486		7312381		7555092		6938319.	797597.1
48	6120063		7475092		8384355		7326503.	930345.2
72	6170299		7741562		7999198		7303686.	808298.2

Formulation	Wt.%
Chlorhexidine	30
Propylene Glycol	6
PEG 300	24
Matrix	40

Date: 01/02/91
File: 4MSTA-45

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031-PDDS1 4 Month Sample @ 38 C/ 90% R.H.

STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	483774	496960	490367
500	3175808	3019575	3097692
800	4972109	5073741	5022925
1000	6270407	6372312	6321360
2000	12105367	11985874	12045621

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	246.0	246.0	696.1	696.1
1	437.4	443.5	1255.1	559.1
2	580.2	591.2	1673.0	417.9
4	732.9	747.4	2115.1	442.0
8	1109.7	1128.0	3192.2	1077.1
24	1315.9	1343.7	3802.6	610.4
48	1458.9	1491.8	4221.9	419.3
72	1409.3	1445.8	4091.5	-130.4

Regression Output:

Constant	40097.48	4 MONTH STABILITY
Std Err of Y Est	162188.6	38 C/90% RH
R Squared	0.998935	
No. of Observations	6	
Degrees of Freedom	4	

X Coefficient(s) 6076.676
Std Err of Coef. 99.19593

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	1555953	1522395	1577638	1642328	1422335	1487558	1534701.	69376.77
1	2699292		3022119		2372003		2697804.	265410.8
2	3420408		3741443		3536285		3566045.	132740.6
4	5193744		4224488		4062155		4493462.	499589.0
8	7064459		6485492		6799499		6783150	236644.8
24	8873812		7300184		7435609		8036535	610466.1
48	10998284		7981894		7736483		8905553.	1483171.
72	8239171		10233255		7339333		8603919.	1209263.

Formulation	Wt.%
Chlorhexidine	30
Propylene Glycol	6
PEG 300	24
Matrix	40

Date: 01/02/91
File: 4MSTA-38.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031-PDDS1 4 Month Sample @ RT

STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	483774	496960	490367
500	3175808	3019575	3097692
800	4972109	5073741	5022925
1000	6270407	6372312	6321360
2000	12105367	11985874	12045621

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	400.6	400.6	1133.6	1133.6
1	493.0	503.0	1423.5	289.9
2	651.8	664.1	1879.4	455.9
4	929.4	945.7	2676.3	796.9
8	1414.9	1438.2	4070.0	1393.7
24	1530.8	1566.2	4432.4	362.4
48	1572.0	1610.2	4557.0	124.6
72	1623.7	1663.0	4706.4	149.4

Regression Output:

Constant	40097.48	4 MONTH STABILITY
Std Err of Y Est	162188.6	ROOM TEMPERATURE
R Squared	0.998935	
No. of Observations	6	
Degrees of Freedom	4	
X Coefficient(s)	6076.676	
Std Err of Coef.	99.19593	

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	2475505	2579576	2786440	2797086	2099471	2107149	2474204.	285190.9
1	3100808		3013634		2992924		3035788.	46746.55
2	3814916		4263113		3924233		4000754	190808.3
4	5467471		6474483		5121392		5687782	573943.3
8	9389366		8761175		7763876		8638139	669282.1
24	9243781		10087644		8696030		9342485	572395.1
48	9218143		9297848		10261347		9592448	474100.8
72	9229983		11739188		8751998		9907056.	1310126.

Formulation	Wt.%
Chlorhexidine	30
Propylene Glycol	6
PEG 300	24
Matrix	40

Date: 01/03/91
File: 4MSTA-RT.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031-PDDS1 4 Month Sample @ RT Under Water

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STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	483774	496960	490367
500	3175808	3019575	3097692
800	4972109	5073741	5022925
1000	6270407	6372312	6321360
2000	12105367	11985874	12045621

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	365.5	365.5	1034.3	1034.3
1	495.7	504.8	1428.7	394.4
2	677.8	690.2	1953.2	524.5
4	905.5	922.5	2610.6	657.4
8	1324.3	1346.9	3811.8	1201.3
24	1572.0	1605.1	4542.6	730.7
48	1680.4	1719.7	4866.7	324.1
72	1661.8	1703.8	4821.8	-44.9

Regression Output:

Constant	40097.48	4 MONTH STABILITY
Std Err of Y Est	162188.6	23 C UNDER WATER
R Squared	0.998935	
No. of Observations	6	
Degrees of Freedom	4	

X Coefficient(s) 6076.676
Std Err of Coef. 99.19593

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	2198547	2110351	2569691	2534382	2088199	2064325	2260915.	210223.9
1	2925105		3463422		2768320		3052282.	297682.4
2	4115787		4301791		4058718		4158765.	103783.3
4	5810866		5596235		5220913		5542671.	243807.2
8	8192582		7385759		8084056		8087465.	84469.55
24	9677735		9216571		9884328		9592884.	279138.0
48	11125597		9588555		10039492		10251214	645106.9
72	10829619		9539690		10045546		10138285	530678.5

Formulation	Wt.%
Chlorhexidine	30
Propylene Glycol	6
PEG 300	24
Matrix	40

Date: 01/02/91
File: 4MSTA-RW.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031-PDDS1 4 Month Sample @ - 40 C

STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	483774	496960	490367
500	3175808	3019575	3097692
800	4972109	5073741	5022925
1000	6270407	6372312	6321360
2000	12105367	11985874	12045621

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	385.4	385.4	1090.6	1090.6
1	571.0	580.6	1643.1	552.5
2	735.5	749.7	2121.8	478.7
4	1081.3	1099.7	3112.2	990.4
8	1430.0	1457.0	4123.5	1011.3
24	1686.8	1722.5	4874.7	751.3
48	1697.3	1739.4	4922.6	47.9
72	1590.3	1632.7	4620.6	-302.0

Regression Output:

Constant	40097.48	4 MONTH STABILITY
Std Err of Y Est	162188.6	-40 C
R Squared	0.998935	
No. of Observations	6	
Degrees of Freedom	4	

X Coefficient(s) 6076.676
Std Err of Coef. 99.19593

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	2130814	2121731	2378740	2518736	2596571	2544532	2381854	192353.3
1	3382603		3682870		3463445		3509639.	126860.8
2	4473437		4525618		4528844		4509299.	25392.91
4	6448878		6382939		7000937		6610918	277095.7
8	8096432		9427615		8665500		8729849	545354.7
24	9960974		11171996		9737083		10290017	630315.3
48	9600819		12107873		9353078		10353923	1244346.
72	9313029		10725875		9072647		9703850.	729313.2

Formulation	Wt.%
Chlorhexidine	30
Propylene Glycol	6
PEG 300	24
Matrix	40

Date: 01/02/91
File: 4MSTA-40.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031-PDDS1 6 Month Sample @ 45 C/90% RH

STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	468111	466557	467334
500	2197937	2159838	2178888
800	3823419	3861757	3842588
1000	4786595	4731125	4758860
2000	11213550	11120588	11167069

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif mcg/cm2
0.0	0.0	0.0	0.0	0.0
0.5	256.3	256.3	725.2	725.2
1	398.0	401.9	1137.3	412.1
2	475.7	481.6	1363.1	225.8
4	568.1	575.3	1628.0	265.0
8	858.0	866.5	2452.3	824.3
24	1226.4	1239.3	3507.2	1054.9
48	1374.6	1393.0	3942.2	435.0
72	1310.9	1331.5	3768.3	-173.9

Regression Output:

Constant	-342102.	6 MONTH STABILITY
Std Err of Y Est	412264.6	45 C/90% RH
R Squared	0.991842	
No. of Observations	6	
Degrees of Freedom	4	
X Coefficient(s)	5560.782	
Std Err of Coef.	252.1445	

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	1009789	996879	1043022	1032641	1170294	1244917	1082923.	91967.62
1	1574676		1949058		2090036		1871256.	217468.4
2	1676694		2379839		2852522		2303018.	483093.4
4	1977629		3689380		2784457		2817155.	699201.8
8	2601752		5205182		5480242		4429058.	1296971.
24	4911387		8959730		7562015		6477710.	1134523.
48	6701965		7087593		8115738		7301765.	596708.1
72	6471697		7527608		6843511		6947605.	437312.8

Formulation	Wt.%
Chlorhexidine	30
Propylene Glycol	6
PEG 300	24
Matrix	40

Date: 02/26/91
File: 6MSTA-45.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031-PDDS1 6 Month Sample @ 38 C/90% RH

STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	468111	466557	467334
500	2197937	2159838	2178888
800	3823419	3861757	3842588
1000	4786595	4731125	4758860
2000	11213550	11120588	11167069

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	383.0	383.0	1084.0	1084.0
1	466.1	471.8	1335.3	251.3
2	557.2	564.2	1596.6	261.4
4	787.6	796.0	2252.6	656.0
8	1122.6	1134.4	3210.4	957.8
24	1348.7	1365.6	3864.5	654.1
48	1289.5	1309.7	3706.5	-158.0
72	1515.3	1534.6	4342.9	636.4

Regression Output:

Constant	-342102.	6 MONTH STABILITY
Std Err of Y Est	412264.6	38 C/90% RH
R Squared	0.991842	
No. of Observations	6	
Degrees of Freedom	4	

X Coefficient(s) 5560.762
Std Err of Coef. 252.1445

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	2032165	2223901	1677148	1760453	1469470	1503915	1787842	282175.6
1	2266486		2401124		2081271		2249627	131122.4
2	3352777		2469674		2446307		2756252.	421914.2
4	4892261		3446749		3774163		4037724.	818856.2
8	6747489		5254448		5699426		5900454.	625887.1
24	7484229		7379074		6610054		7157785.	389676.6
48	7412122		7007982		6065073		6828392.	564402.0
72	9202462		7964303		7084958		8083907.	868594.5

Formulation	Wt.%
Chlorhexidine	30
Propylene Glycol	6
PEG 300	24
Matrix	40

Date: 02/28/91
File: 6MSTA-38.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031-PDDS1 6 Month Sample @ RT

STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	468111	466557	467334
500	2197937	2159838	2178888
800	3823419	3861757	3842588
1000	4786595	4731125	4758860
2000	11213550	11120588	11167069

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif a/cm2
0.0	0.0	0.0	0.0	0.0
0.5	415.7	415.7	1176.4	1176.4
1	558.4	564.6	1597.9	421.5
2	718.4	726.7	2056.7	458.8
4	1007.1	1017.9	2880.5	823.9
8	1369.3	1384.4	3917.8	1037.3
24	1719.9	1740.4	4925.4	1007.6
48	1761.6	1787.4	5058.3	132.9
72	1669.1	1695.6	4798.5	-259.9

Regression Output:

Constant	-342102.	6 MONTH STABILITY
Std Err of Y Est	412264.6	ROOM TEMPERATURE
R Squared	0.991842	
No. of Observations	6	
Degrees of Freedom	4	

X Coefficient(s) 5560.782
Std Err of Coef. 252.1445

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	2015344	2196492	1888163	1801489	1919087	1995582	1969359.	123620.4
1	2469263		2549557		3270177		2762999	360123.9
2	3707421		3629135		3621104		3652553.	38935.58
4	5161096		5147881		5465163		5258046.	146552.6
8	7328602		7107940		7379882		7272141.	117980.1
24	9686430		8372149		9606579		9221719.	801620.7
48	8871077		10295870		9194121		9453689.	609940.1
72	8343151		9230042		9245659		8939619.	421815.1

Formulation	Wt.%
Chlorhexidine	30
Propylene Glycol	6
PEG 300	24
Matrix	40

Date: 03/08/91
File: 6MSTA-RT.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 908031-PDDS1 6 Month Sample @ 2T/WATER

STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	468111	466557	467334
500	2197937	2159838	2178888
800	3823419	3861757	3842588
1000	4786595	4731125	4758860
2000	11213550	11120588	11167069

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	341.5	341.5	966.4	966.4
1	606.7	611.9	1731.5	765.2
2	743.4	752.5	2129.6	398.1
4	1052.6	1063.8	3010.5	880.9
8	1619.7	1635.4	4628.3	1617.8
24	1868.9	1893.2	5357.8	729.5
48	2117.9	2146.0	6073.1	715.3
72	2043.9	2075.7	5874.1	-199.0

Regression Output:

Constant	-342102.	6 MONTH STABILITY
Std Err of Y Est	412264.6	23 CUNDER WATER
R Squared	0.991842	
No. of Observations	6	
Degrees of Freedom	4	
X Coefficient(s)	5560.762	
Std Err of Coef.	252.1445	

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	1092069	1132431	1819236	1824720	1824720	1601975	1556790	318902.3
1	2833779		3073257		3188331		3031789	147685.4
2	3964774		3521818		3888913		3791835	193426.3
4	5288056		5136404		5109667		5511375.	427562.0
8	8179055		10024860		7789272		8664395.	975065.8
24	9833503		13004202		7253864		10050523	2350189.
48	10569555		12296671		11439417		11435214	705098.4
72	11021978		10588402		10859959		11023446	437504.9

Formulation	Wt.%
Chlorhexidine	30
Propylene Glycol	6
PEG 300	24
Matrix	40

Date: 02/28/91
File: GMSTA-RW.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031-PDDS1 6 Month Sample @ - 40 C

STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	468111	466557	467334
500	2197937	2159838	2178888
800	3823419	3861757	3842588
1000	4786595	4731125	4758860
2000	11213550	11120588	11167069

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	462.7	462.7	1309.4	1309.4
1	588.5	595.4	1685.0	375.6
2	709.6	718.5	2033.2	348.3
4	981.8	992.4	2808.6	775.3
8	1275.1	1289.8	3650.1	841.5
24	1534.7	1553.9	4397.4	747.4
48	1560.8	1583.9	4482.3	84.9
72	1758.0	1781.4	5041.5	559.1

Regression Output:

Constant	-342102.	6 MONTH STABILITY
Std Err of Y Est	412264.6	-40 C
R Squared	0.991842	
No. of Observations	6	
Degrees of Freedom	4	

X Coefficient(s) 5560.762
Std Err of Coef. 252.1445

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	2349318	2259408	2360281	2405449	1977451	2032281	2230698	166196.6
1	2822315		3298349		2669804		2930156	267693.1
2	3673438		4323118		2815447		3604001	617459.3
4	5500934		6121526		3729713		5117391	1013417.
8	7509981		7264724		5469863		6748189.	909441.7
24	8395600		8653446		7527666		8192237.	481568.5
48	8934111		7885349		8192598		8337352.	440220.2
72	9119582		10613321		8563564		9433822.	863835.6

Formulation	Wt.%
Chlorhexidine	30
Propylene Glycol	6
PEG 300	24
Matrix	40

Date: 02/26/91
File: 6MSTA-40.WK1

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PDDS2 Set 1

STANDARD CALIBRATION CURVE
= 254 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
1	47448	49780	48614
5	281594	286471	284033
10	568117	576598	572358
15	833426	847205	840316

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif mcg/cm2
0.0	0.0	0.0	0.0	0.0
0.5	2.9	2.9	8.3	8.3
1	4.2	4.3	12.1	3.8
2	6.4	6.5	18.3	6.1
4	9.2	9.4	26.6	8.3
8	11.2	11.5	32.5	5.9
24	12.2	12.4	35.2	2.8
48	14.0	14.3	40.5	5.3
72	13.8	14.2	40.0	-0.5

Regression Output:

Constant	-1388.48
Std Err of Y Est	7360.972
R Squared	0.999679
No. of Observations	5
Degrees of Freedom	3

X Coefficient(s) 56524.57
Std Err of Coef. 584.1305

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	172125	162597	160724	165148.6	4991.923
1	232959	251906	226010	236958.3	10943.69
2	354554	360935	358230	357906.3	2615.066
4	523156	510231	526826	520071	7117.416
8	649196	675252	577233	633893.6	41453.20
24	694514	703979	659998	686163.6	18901.11
48	837370	741313	792565	790416	39244.53
72	759865	815255	760980	778700	25852.29

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 11/26/90
File: SD101811.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PPDS2 Set 1

STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	655604	501975	578790
500	2989292	3056439	3022866
800	4953288	4817120	4885204
1000	5927591	5857809	5892700
2000	12004674	12281809	12143242

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	110.1	110.1	311.6	311.6
1	147.6	150.4	425.6	114.0
2	213.4	217.1	614.5	188.9
4	320.3	325.6	921.5	307.0
8	441.0	449.1	1270.8	349.3
24	508.8	519.9	1471.2	200.4
48	747.5	760.2	2151.4	680.2
72	762.1	780.8	2209.7	58.3

Regression Output:

Constant	-25235.1
Std Err of Y Est	82715.81
R Squared	0.999721
No. of Observations	6
Degrees of Freedom	4

X Coefficient(s) 6062.320
Std Err of Coef. 50.58968

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	779832	754930	522647	569581	628037	598822	642318.1	94262.70
1	1008822		735491		805256		869856.3	98344.39
2	1522727		1140880		1142635		1268747.	179592.1
4	2177481		1766784		1805256		1916507	185293.6
8	2875241		2532709		2537589		2648513	160333.2
24	4070036		2577678		2530707		3059473.	714832.7
48	4568508		4689061		4261474		4506347.	180010.3
72	4662512		4695151		4427337		4595000	119302.1

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 11/12/90
File: C0101811.WK1

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PDDS2 Set 2

STANDARD CALIBRATION CURVE
= 254 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
1	47448	49780	48614
5	281594	286471	284033
10	568117	576598	572358
15	833426	847205	840316

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	2.7	2.7	7.6	7.6
1	4.3	4.3	12.3	4.7
2	5.8	5.9	16.8	4.5
4	9.0	9.2	26.0	9.2
8	11.6	11.8	33.4	7.4
24	12.8	13.1	37.2	3.8
48	14.3	14.6	41.4	4.2
72	12.8	13.1	37.2	-4.2

Regression Output:

Constant	-1388.48
Std Err of Y Est	7360.972
R Squared	0.999679
No. of Observations	5
Degrees of Freedom	3

X Coefficient(s) 56524.57
Std Err of Coef. 584.1305

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	156481	149805	144629	150305	4851.458
1	256043	230484	233125	239884	11476.89
2	335883	313159	333666	327569.3	10229.76
4	521096	501791	505004	509297	8445.635
8	668402	657800	631563	652588.3	15484.38
24	865599	803376	704010	724328.3	108011.8
48	888498	747036	785088	806874	59770.93
72	785088	667302	710541	720977	48648.86

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 11/26/90
File: S0101812.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PPDS2 Set 2

STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	655604	501975	578790
500	2989292	3056439	3022866
800	4953288	4817120	4885204
1000	5927591	5857809	5892700
2000	12004674	12281809	12143242

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	87.6	87.6	247.8	247.8
1	127.8	129.9	367.7	119.9
2	188.9	192.0	543.5	175.8
4	295.9	300.6	850.7	307.2
8	413.3	420.7	1190.4	339.8
24	608.4	618.7	1751.0	560.6
48	691.8	707.0	2000.9	249.9
72	707.5	724.8	2051.3	50.4

Regression Output:

Constant	-25235.1
Std Err of Y Est	82715.81
R Squared	0.999721
No. of Observations	6
Degrees of Freedom	4
X Coefficient(s)	6062.320
Std Err of Coef.	50.58968

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	409141	464281	634469	637809	450776	437715	505695.1	93731.60
1	340500		792349		614833		749227.3	97042.97
2	1121776		1176662		1060535		1119657.	47432.30
4	1792132		1730964		1782181		1768425.	26799.10
8	2517837		2444906		2477399		2480047.	29832.78
24	3495558		3706013		3787610		3663060.	123037.3
48	3993441		4271955		4241134		4168843.	124664.7
72	4160022		4405738		4226442		4264067.	103781.3

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 11/12/90
File: C0101812.WK1

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 910181-PDDS2 2 Month Stability 45 C

STANDARD CALIBRATION CURVE
= 254 nm

mcg/ml	AUC	ACC	AVGAUC
0	0	0	0
1	770	764	767
5	3989	4124	4057
10	8798	8425	8612
15	12552	12799	12676

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	4.5	4.5	12.8	12.8
1	6.7	6.8	19.2	6.4
2	10.1	10.3	29.2	10.0
4	14.2	14.5	41.0	11.8
8	18.8	19.1	54.2	13.2
24	27.5	28.0	79.1	24.9
48	33.6	34.3	97.0	17.9
72	35.6	36.5	103.2	6.2

Regression Output:

Constant	-64.7625	
Std Err of Y Est	128.6688	2 MONTH STABILITY
R Squared	0.999570	45 C/ 90% RH
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 852.7197
Std Err of Coef. 10.21052

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	3607	3540	3876	4008	3902	3809	3790.333	165.2338
1	4636		6253		5969		5619.333	794.3219
2	7989		9181		8585		8585	486.6319
4	10808		13646		11729		12061	1182.153
8	13160		18272		16448		15960	2115.300
24	24385		23191		22530		23368.66	787.6502
48	25851		30164		29714		28576.33	1935.838
72	27440		31678		31811		30309.66	2029.887

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 01/09/91
File: S2MSTA45.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 910181-PPDS2 2 MONTH @ 45 C/90% RH

STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	465030	447428	456229
500	3001352	3052565	3026959
800	5119063	5211993	5165528
1000	6908573	6631426	6770000

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	87.2	87.2	246.7	246.7
1	155.1	157.3	445.2	198.5
2	232.6	236.4	669.1	223.9
4	330.7	336.5	952.4	283.3
8	452.8	461.1	1304.8	352.3
24	630.5	641.8	1816.3	511.5
48	726.5	742.3	2100.7	284.4
72	740.9	759.0	2148.1	47.4

Regression Output:

Constant	-163662.	2 MONTH STABILITY
Std Err of Y Est	184491.5	45 C/90% RH
R Squared	0.997026	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 6765.428
Std Err of Coef. 213.3171

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	438012	435816	496994	473073	361884	350800	426096.5	53638.45
1	884011		969801		803735		885869	67784.39
2	1433205		1568652		1227359		1409738.	140316.8
4	2037815		2289375		1894481		2073890.	163220.4
8	3133861		2971175		2593790		2899608.	226215.9
24	4364562		4144148		3796441		4101717	233866.9
48	5230710		4428854		4595318		4751627.	345511.9
72	5281538		4897269		4367225		4848677.	374844.7

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 01/09/91
File: CZMSTA45.WK1

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PDDS2 2 Month Stability 38 C/90

STANDARD CALIBRATION CURVE
= 254 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
1	782	800	791
5	4161	4152	4157
10	8258	8516	8387
15	13565	13380	13473
25	22423	21531	21977
50	44646	43836	44241

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	5.5	5.5	15.5	15.5
1	8.0	8.2	23.1	7.6
2	11.7	11.9	33.6	10.6
4	12.5	12.8	36.1	2.5
8	14.1	14.4	40.9	4.7
24	19.8	20.2	57.0	16.2
48	25.2	25.7	72.7	15.7
72	28.4	29.0	82.1	9.4

Regression Output:

Constant	-149.643
Std Err of Y Est	226.6197
R Squared	0.999825
No. of Observations	7
Degrees of Freedom	5

X Coefficient(s) 887.4764
Std Err of Coef. 5.239349

2 MONTH STABILITY
38 C/90% RH

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	5024	5193	5093	5118	3863	3904	4699.166	578.9903
1	7133		7266		6516		6971.666	326.7479
2	9723		11854		9097		10224.66	1180.117
4	11011		11482		10273		10922	497.5680
8	11610		14453		11110		12391	1472.273
24	17784		17331		16952		17422.33	348.2454
48	23335		24007		19284		22208.66	2086.169
72	24501		27912		22679		25030.66	2168.944

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 01/14/91
File: S2MSTA38.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PPDS2 2 MONTH @ 38 C/90% RH

STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	465030	447428	456229
500	3001352	3052565	3026959
800	5119063	5211993	5165528
1000	6908573	6631426	6770000

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	87.1	87.1	246.5	246.5
1	150.5	152.7	432.2	185.7
2	217.4	221.2	626.0	193.9
4	278.8	284.3	804.5	178.5
8	371.7	378.7	1071.6	267.1
24	535.2	544.5	1540.8	469.2
48	599.4	612.8	1734.3	193.5
72	615.0	630.0	1782.9	48.6

Regression Output:

Constant	-163662.	2 MONTH STABILITY
Std Err of Y Est	184491.5	38 C/90% RH
R Squared	0.997026	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 6765.428
Std Err of Coef. 213.3171

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	337321	322280	486690	479378	464570	463061	425550	68330.37
1	757689		952895		853614		854732.6	79696.44
2	1131350		1463441		1327534		1307441.	136317.3
4	1679766		1781834		1706926		1722842	43162.16
8	2270738		2512471		2269788		2350999	114178.6
24	3474070		3619887		3276830		3456929	140575.9
48	3698102		4281226		3696278		3891868.	275318.2
72	4042276		4148821		3800297		3997131.	145821.2

Formulation	Wt.%	Date:	01/09/91
Silver sulfadiazine	20	File:	C2MSTA38.WK1
Chlorhexidine gluconate	10		
Pluronic L-62	20		
Matrix	50		

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's S.N. 910181-PDDS2 2 Month Stability RT/RATE

STANDARD CALIBRATION CURVE
= 254 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
1	782	800	791
5	4161	4152	4157
10	8258	8516	8387
15	13565	13380	13473
25	22423	21531	21977
50	44646	43836	44241

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	3.2	3.2	8.9	8.9
1	5.7	5.8	16.5	7.5
2	8.9	9.1	25.7	9.2
4	7.6	7.8	22.2	-3.5
8	8.8	9.0	25.5	3.3
24	10.8	11.0	31.2	5.7
48	13.3	13.6	38.4	7.2
72	15.6	15.9	45.1	6.8

Regression Output:

Constant	-149.643	
Std Err of Y Est	226.6197	2 MONTH STABILITY
R Squared	0.999825	ROOM TEMPERATURE
No. of Observations	7	
Degrees of Freedom	5	

X *Coefficient(s)* 887.4764
Std Err of Coef. 5.239349

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	2654	2535	2701	2717	2666	2665	2656.333	58.33338
1	4775		5067		5017		4953	127.5094
2	7454		8104		7776		7778	265.3651
4	6120		7348		6370		6612.666	529.8813
8	9014		7425		6595		7678	1003.625
24	9098		9626		9578		9434	238.2046
48	11707		11417		11862		11662	184.4360
72	13445		14045		13581		13690.33	256.8596

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 01/14/91
File: S2MSTART.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PPDS2 2 MONTH @ RT

STANDARD CALIBRATION CURVE
= 238 nm

ncg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	436694	421586	429140
500	2959605	3014962	2987284
800	5224554	5168120	5196337
1000	5808496	5811411	5809954

Data of Average Values

Hr.	ncg/ml	dil adj ncg/ml	ncg/cm2	dif x/cm2
0.0	0.0	0.0	0.0	0.0
0.5	92.5	92.5	261.8	261.8
1	159.7	162.1	458.6	196.8
2	208.9	212.9	602.5	143.8
4	317.9	323.2	914.5	312.1
8	410.8	418.7	1185.0	270.4
24	605.2	615.5	1741.9	556.9
48	674.1	689.2	1950.4	208.6
72	720.0	736.8	2085.2	134.8

Regression Output:

Constant	-163662.	2 MONTH STABILITY
Std Err of Y Est	184491.5	ROOM TEMPERATURE
R Squared	0.997026	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 6765.428
Std Err of Coef. 213.3171

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	450697	469649	459372	462167	463282	468356	462253.8	6256.335
1	322764		375106		853426		517098.6	49836.31
2	1262778		1331913		1154091		1249594	73191.66
4	2026374		1969276		1966305		1987318.	27643.14
8	2618422		2712807		2514755		2615331.	80884.11
24	3744503		4168256		3880282		3931013.	176676.5
48	4071187		4712747		4406188		4396707.	262001.5
72	4758075		4836427		4527481		4707327.	131131.9

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 01/14/91
File: C2MSTART.WK1

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PDDS2 2 Month Stability RT/WATE

STANDARD CALIBRATION CURVE
= 254 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
1	782	800	791
5	4161	4152	4157
10	8258	8516	8387
15	13565	13380	13473
25	22423	21531	21977
50	44646	43836	44241

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	Dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	3.0	3.0	8.6	8.6
1	5.9	6.0	16.8	8.2
2	9.0	9.1	25.8	8.9
4	10.1	10.3	29.3	3.5
8	9.3	9.6	27.1	-2.2
24	12.1	12.4	35.0	7.9
48	15.1	15.4	43.5	8.5
72	16.1	16.5	46.6	3.1

Regression Output:

Constant	-149.643
Std Err of Y Est	226.6197
R Squared	0.999825
No. of Observations	7
Degrees of Freedom	5

2 MONTH STABILITY
23 C UNDER WATER

X Coefficient(s) 887.4764
Std Err of Coef. 5.233349

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	2532	2448	2525	2511	2557	2613	2547.666	60.35311
1	4935		5307		4993		5065	175.7346
2	7660		7840		7909		7803	104.3666
4	9550		7756		10204		9836.666	1019.741
8	8481		7925		8588		8121.333	585.3324
24	10646		9755		11452		10617.66	893.0869
48	12403		14066		13190		13219.66	879.2409
72	14091		14707		13593		14130.33	455.6382

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 01/14/91
File: SZHSTABW.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PPDS2 2 MONTH @ RT/WATER

STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	465030	447428	456229
500	3001352	3052565	3026959
800	5119063	5211993	5165528
1000	6908573	6631426	6770000

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	104.0	104.0	294.3	294.3
1	157.1	159.7	452.1	157.7
2	211.2	215.1	608.7	156.7
4	326.7	332.0	939.6	330.9
8	425.4	433.5	1226.9	287.2
24	602.0	612.6	1733.6	506.8
48	663.5	678.5	1920.2	186.6
72	693.3	709.9	2009.0	88.8

Regression Output:

Constant	-163662.	2 MONTH STABILITY
Std Err of Y Est	184491.5	23 C UNDER WATER
R Squared	0.397026	
No. of Observations	5	
Degrees of Freedom	3	
X Coefficient(s)	6765.428	
Std Err of Coef.	213.3171	

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	613842	611716	491108	466885	523902	532468	539986.8	55749.33
1	850732		390842		956805		899459.6	43730.75
2	1243265		1220185		1331519		1264989.	47977.87
4	2053341		1862753		2224664		2046919.	147819.3
8	2825287		2547879		2768888		2714018	119713.0
24	4036382		3775010		3915220		3908874	106799.2
48	4601779		3887557		4485757		4325031	312946.1
72	4735352		4010247		4834986		4526861.	367559.3

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 01/09/91
File: C2MSTABW.WK1

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PDDS2 2 Month Stability -40 C

STANDARD CALIBRATION CURVE
= 254 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
1	770	764	767
5	3989	4124	4057
10	8798	8425	8612
15	12552	12799	12676

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	2.5	2.5	7.1	7.1
1	4.8	4.9	13.9	6.8
2	6.7	6.8	19.2	5.3
4	9.3	9.5	26.9	7.7
8	12.4	12.7	35.8	8.9
24	11.6	11.9	33.7	-2.1
48	13.4	13.7	38.9	5.2
72	15.2	15.5	44.0	5.1

Regression Output:

Constant	-64.7625	2 MONTH STABILITY
Std Err of Y Est	128.6688	-40 C
R Squared	0.999570	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 852.7197
Std Err of Coef. 10.21052

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	2073	2131	1989	2025	2143	2088	2074.833	54.51121
1	4013		3885		4478		4058.666	325.3473
2	5892		5490		5470		5617.333	194.3902
4	8158		7973		7575		7902	242.2461
8	10436		10251		10888		10525	267.5605
24	9994		9696		9746		9812	130.3022
48	11874		10899		11429		11400.66	338.5459
72	12072		12846		13788		12902	701.6722

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 01/09/91
File: S2MSTA40.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PPDS2 2 MONTH @ -40 C

STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	465030	447428	456229
500	3001352	3052565	3026959
800	5119063	5211993	5165528
1000	6908573	6631426	6770000

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	102.7	102.7	290.6	290.6
1	161.8	164.4	465.1	174.6
2	226.6	230.7	652.9	187.7
4	324.7	330.4	935.0	282.2
8	447.0	455.2	1288.1	353.1
24	613.4	624.6	1767.6	479.4
48	680.7	696.0	1969.7	202.1
72	746.0	763.0	2159.4	189.8

Regression Output:

Constant	-163662.	2 MONTH STABILITY
Std Err of Y Est	184491.5	-40 C
R Squared	0.997026	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 6765.428
Std Err of Coef. 213.3171

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	587867	574502	564279	547428	452120	459891	531014.5	54439.86
1	993647		904004		895194		930948.3	44480.30
2	1356657		1391807		1360653		1369705.	15712.31
4	1952977		2116238		2030674		2033296.	66676.31
8	2763011		2973739		2845709		2860819.	86690.33
24	3928171		4000032		4030719		3986307.	42975.17
48	4196734		4180455		4946686		4441291.	357429.5
72	4642974		4735465		5272224		4883554.	277412.7

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 01/09/91
File: C2MSTA40.WK1

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PDDS2 4 Month Stability 45 C/ 9

STANDARD CALIBRATION CURVE
= 254 nm

ucg/ml	AUC	AUC	AVGAUC
0	0	0	0
1	1027	1007	1017
10	9630	9816	9723
25	26359	25639	25999
50	50899	49226	50063

Data of Average Values

Hr.	ucg/ml	dil adj ucg/ml	ucg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	7.8	7.8	22.1	22.1
1	10.4	10.6	30.1	8.0
2	14.5	14.7	41.7	11.6
4	17.4	17.7	50.2	8.5
8	23.8	24.2	68.5	18.4
24	33.5	34.1	96.6	28.0
48	43.1	43.9	124.4	27.8
72	49.5	50.5	143.0	18.6

Regression Output:

Constant	46.46175	4 MONTH STABILITY
Std Err of Y Est	539.7304	45 C/90% RH
R Squared	0.999506	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 1006.618
Std Err of Coef. 12.91383

HR.	A cell		B cell			AVG.	STD.
0	0	0	0	0	0	0	0
0.5	5762	6007	9583	9158	8634	8206 7891.666	1483.325
1	8164		11808		11656	10542.66	1683.115
2	12712		16061		15046	14606.33	1402.124
4	15128		19525		17947	17533.33	1818.743
8	21019		26402		24541	23987.33	2232.201
24	32142		36733		32497	33790.66	2085.585
48	40763		45471		44070	43434.66	1973.837
72	49953		51611		47908	49824	1514.492

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 03/11/91
File: S4MSTA45.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PPDS2 4 MONTH @ 45 C/90% RH

STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	463948	457909	460929
500	2197616	2200343	2198980
800	3590139	3733032	3661586
1000	4771401	4665302	4718352
2000	11250345	11273955	11262150

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	157.4	157.4	445.6	445.6
1	212.7	216.6	613.1	167.5
2	270.1	275.4	779.3	166.2
4	362.3	369.0	1044.4	265.0
8	461.9	471.0	1332.9	288.6
24	638.4	650.0	1839.4	506.5
48	718.9	734.9	2079.6	240.2
72	768.3	786.3	2225.1	145.5

Regression Output:

Constant	-387483.	4 MONTH STABILITY
Std Err of Y Est	477216.2	45 C/90% RH
R Squared	0.989239	
No. of Observations	6	
Degrees of Freedom	4	

X Coefficient(s) 5597.022
Std Err of Coef. 291.8634

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	434519	448825	598991	572561	463159	444485	493756.6	66050.81
1	793062		808323		807819		803068	7078.301
2	1123181		1123255		1125681		1124039	1161.462
4	1758602		1540742		1621252		1640198.	89944.34
8	2334226		2160787		2098929		2197980.	99594.83
24	3482369		3219515		2855631		3185838.	256970.4
48	3785907		3642100		3480470		3636159	124764.8
72	4057255		4005006		3675572		3912611	168963.7

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 03/11/91
File: C:\MS\A45.WK1

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PDDS2 4 Month Stability 38 C/ 9

STANDARD CALIBRATION CURVE
= 254 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
1	1027	1007	1017
10	9630	9816	9723
25	26359	25639	25999
50	50899	49226	50063

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	5.8	5.8	16.4	16.4
1	7.7	7.9	22.3	5.9
2	11.5	11.7	33.0	10.7
4	16.2	16.5	46.6	13.6
8	22.0	22.4	63.4	16.8
24	32.2	32.8	92.7	29.3
48	42.2	43.0	121.6	28.9
72	46.1	47.2	133.5	11.9

Regression Output:

Constant	46.46175	4 MONTH STABILITY
Std Err of Y Est	539.7304	38 C/90% RH
R Squared	0.999508	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 1006.618
Std Err of Coef. 12.91383

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	6726	6804	5385	5599	5246	5447	5867.833	643.1737
1	8013		7980		7500		7831	234.4397
2	11796		11865		11112		11591	339.8735
4	16886		15650		16504		16346.66	516.7135
8	22637		22024		21905		22188.66	320.7203
24	33161		32149		32097		32469	489.7781
48	43481		46979		37048		42502.66	4112.909
72	46177		43547		43729		44484.66	2387.035

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 93/10/31
File: S4MSTA38.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PTDS2 4 MONTH @ 38 C/90% RH

STANDARD CALIBRATION CURVE
= 238 nm

ucg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	463948	457909	460929
500	2197616	2200343	2198980
800	3590139	3733032	3661586
1000	4771401	4665302	4718352
2000	11250345	11273955	11262150

Data of Average Values

Hr.	ucg/ml	dil adj ucg/ml	ucg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	155.2	155.2	439.2	439.2
1	211.6	215.4	609.7	170.5
2	285.2	290.5	822.0	212.3
4	377.1	384.3	1087.5	265.5
8	481.0	490.4	1387.9	300.4
24	696.0	708.1	2003.8	615.9
48	764.8	782.2	2213.8	209.9
72	785.5	804.6	2277.0	63.2

Regression Output:

Constant	-387483.	4 MONTH STABILITY
Std Err of Y Est	477216.2	38 C/90% RH
R Squared	0.989239	
No. of Observations	6	
Degrees of Freedom	4	

X Coefficient(s) 5597.022
Std Err of Coef. 291.8694

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	373604	354486	516175	503917	575466	563058	481117.6	86563.48
1	767911		836066		785987		796654.6	28828.51
2	1203622		1242298		1179915		1208635	25706.47
4	1764696		1763945		1641467		1723369.	57914.50
8	2347500		2398115		2168345		2304653.	98574.84
24	3122181		3423668		3979079		3508309.	354909.3
48	3864450		4041324		3774372		3893382	110886.2
72	3825230		4280737		3920376		4008781	196185.6

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 03/11/91
File: C:\MSTA38.WK1

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PDDS2 4 Month Stability @ RT

STANDARD CALIBRATION CURVE
= 254 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
1	1027	1007	1017
10	9630	9816	9723
25	26359	25639	25999
50	50899	49226	50063

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	3.1	3.1	8.9	8.9
1	4.3	4.4	12.3	3.4
2	7.2	7.3	20.8	8.4
4	8.8	9.0	25.6	4.8
8	9.6	9.8	27.8	2.2
24	12.6	12.8	36.3	8.6
48	12.0	12.3	34.8	-1.5
72	18.1	18.4	51.9	17.1

Regression Output:

Constant	46.46175	4 MONTH STABILITY
Std Err of Y Est	539.7304	ROOM TEMPERATURE
R Squared	0.999506	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 1006.618
Std Err of Coef. 12.91383

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	3345	3221	3183	3320	3128	3027	3204	108.9128
1	4153		4557		4346		4352	164.3868
2	7179		7826		6959		7321.333	367.3821
4	9488		7606		9764		8952.666	958.8803
8	12798		8163		8133		9698	2192.065
24	10250		10399		17540		12729.66	3401.363
48	12389		11964		11964		12105.66	200.3462
72	22134		15234		17286		18218	2892.976

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 03/18/91
File: S4MSTART.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PPDS2 4 MONTH @ RT

STANDARD CALIBRATION CURVE
= 238 nm

ucg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	463948	457909	460929
500	2197616	2200343	2198980
800	3590139	3733032	3661586
1000	4771401	4665302	4718352
2000	11250345	11273955	11262150

Data of Average Values

Hr.	ucg/ml	dil adj ucg/ml	ucg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	170.5	170.5	482.6	482.6
1	194.6	198.9	562.8	80.2
2	280.8	285.7	808.6	245.8
4	376.6	383.7	1085.8	277.2
8	494.4	503.8	1425.8	340.1
24	755.1	767.4	2171.9	746.0
48	928.4	947.2	2680.7	508.8
72	959.6	982.8	2781.3	100.6

Regression Output:

Constant	-387483.	4 MONTH STABILITY
Std Err of Y Est	477216.2	ROOM TEMPERATURE
R Squared	0.989239	
No. of Observations	6	
Degrees of Freedom	4	

X Coefficient(s) 5597.022
Std Err of Coef. 291.8694

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	625430	601655	622078	607702	472033	473013	566985.1	67277.48
1	668234		723233		713699		701722	33997.34
2	1215138		1126833		1211254		1184408.	40742.77
4	1777160		1787343		1597328		1720610.	87272.84
8	2470242		2385835		2283246		2379774.	76460.99
24	4094626		3754148		3667406		3838726.	184380.7
48	5057604		5151629		4216463		4808565.	420435.5
72	5134558		5103613		4711922		4983364.	122354.0

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 03/18/91
File: C4MSTART.WK1

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's N.W. 010181 PDDS2 4 Month Stability RT/W

STANDARD CALIBRATION CURVE
= 254 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
1	1027	1007	1017
10	9630	9816	9723
25	26359	25639	25999
50	50899	49226	50063

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	3.3	3.3	9.3	9.3
1	5.2	5.2	14.8	5.5
2	7.9	7.9	22.3	7.4
4	9.9	9.9	28.1	5.9
8	11.8	12.1	34.1	6.0
24	14.8	15.1	42.6	8.5
48	13.8	14.1	40.0	-2.7
72	20.4	20.8	58.8	18.8

Regression Output:

Constant	46.46175	4 MONTH STABILITY
Std Err of Y Est	539.7304	23 C UNDER WATER
R Squared	0.999506	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 1006.618
Std Err of Coef. 12.01383

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	3499	3414	3569	3593	3008	3103	3364.333	227.3203
1	4608		5765		5357		5243.333	479.1327
2	7704		8272		7526		7834	318.1236
4	9336		10897		9345		9859.333	733.7503
8	12928		10973		12008		11935.66	1183.009
24	12708		16599		15451		14919.33	1922.375
48	13592		15461		12650		13901	1168.201
72	15420		24836		21596		20617.33	3305.359

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 03/13/91
File: S4MSTARW.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PPDS2 4 MONTH @ RT/WATER

STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	463948	457909	460929
500	2197616	2200343	2198980
800	3590139	3733032	3661586
1000	4771401	4665302	4718352
2000	11250345	11273955	11262150

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	161.3	161.3	456.6	456.6
1	197.8	201.8	571.2	114.6
2	279.9	284.8	806.1	234.9
4	379.6	386.6	1094.0	288.0
8	516.8	526.3	1489.4	395.4
24	731.4	744.3	2106.5	617.1
48	802.4	820.7	2322.5	216.0
72	834.8	854.8	2419.2	96.7

Regression Output:

Constant	-387483.	4 MONTH STABILITY
Std Err of Y Est	477216.2	23 C UNDER WATER
R Squared	0.989239	
No. of Observations	6	
Degrees of Freedom	4	

X Coefficient(s) 5597.022
Std Err of Coef. 291.8694

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	616141	586962	488110	483666	460776	457231	515481	62435.34
1	715972		686365		756297		719544.6	28661.17
2	1077943		1238188		1220954		1179028.	71823.56
4	1519379		1768933		1922896		1737069.	166268.7
8	2239453		2633060		2642658		2505057	187851.2
24	3155912		3964365		3998657		3706311.	389442.8
48	3630073		4235595		4444882		4103516.	345506.3
72	3656226		4557644		4640624		4284831.	445730.1

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 03/11/91
File: C4MSTABW.WK1

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PDDS2 4 Month Stability -40 C

STANDARD CALIBRATION CURVE
= 254 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
1	1027	1007	1017
10	9630	9816	9723
25	26359	25639	25999
50	50899	49226	50063

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	2.9	2.9	8.1	8.1
1	4.2	4.3	12.1	4.0
2	5.7	5.8	16.5	4.4
4	7.6	7.8	22.0	5.5
8	9.1	9.3	26.2	4.2
24	12.3	13.0	36.3	10.7
48	13.9	14.3	40.4	3.5
72	17.1	17.4	49.2	8.9

Regression Output:

Constant	46.46175	4 MONTH STABILITY
Std Err of Y Est	539.7304	-40 C
R Squared	0.999506	ACTUAL TEMP = -23 C
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 1006.618
Std Err of Coef. 12.91383

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	2977	2983	2893	2943	2956	2784	2922.666	68.58733
1	4573		4142		4140		4285	203.6483
2	5709		5846		5892		5815.666	77.72744
4	7605		7822		7731		7719.333	88.97315
8	9373		8941		9187		9167	176.9293
24	9744		15016		14014		12924.66	2285.968
48	12152		17029		13051		14077.33	2119.166
72	18504		13299		19834		17212.33	2819.312

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 03/11/91
File: S4MSTA40.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PPDS2 4 MONTH @ -40 C

STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	463948	457909	460929
500	2197616	2200343	2198980
800	3590139	3733032	3661586
1000	4771401	4665302	4718352
2000	11250345	11273955	11262150

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	159.1	159.1	450.2	450.2
1	206.4	210.4	595.5	145.3
2	272.7	277.8	786.3	190.8
4	371.6	378.4	1071.0	284.7
8	521.0	530.3	1500.7	429.7
24	733.2	746.2	2111.7	611.0
48	808.2	826.5	2339.1	227.4
72	867.5	887.7	2512.1	173.0

Regression Output:

Constant	-387483.	4 MONTH STABILITY
Std Err of Y Est	477216.2	-40 C
R Squared	0.989239	
No. of Observations	6	
Degrees of Freedom	4	

X Coefficient(s) 5597.022
Std Err of Coef. 291.8634

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	461681	469303	457415	430123	597657	600915	502849	69256.71
1	809629		724963		769402		767998	34579.00
2	1035501		1247248		1133224		1138657.	86530.69
4	1604559		1798627		1674188		1692458	80274.28
8	2409548		2600599		2575445		2528530.	84757.83
24	3768572		3729410		3649957		3715979.	49346.79
48	4105050		4130792		4172205		4136015.	27663.61
72	4335746		4423862		4643550		4467719.	129430.6

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Phenolic 2-02	20
Matrix	50

Date: 03/11/91
File: C4MSTA40.WK1

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PDDS2 6 Month Stability 45 C/ 9

STANDARD CALIBRATION CURVE
= 254 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
1	894	980	937
10	10153	10276	10215
25	27109	25930	26520
50	55408	55359	55384

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	7.5	7.5	21.3	21.3
1	11.2	11.3	31.9	10.6
2	15.2	15.4	43.6	11.7
4	19.8	20.0	56.7	13.1
8	24.6	24.9	70.6	13.9
24	33.5	33.9	95.9	25.3
48	40.6	41.1	116.2	20.3
72	47.3	47.9	135.7	19.5

Regression Output:

Constant	-439.341	6 MONTH STABILITY
Std Err of Y Est	625.6089	45 C/90% RH
R Squared	0.999452	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 1107.572
Std Err of Coef. 14.96860

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	10972	11053	5834	5852	6880	6871	7910.333	2233.825
1	17233		8590		9950		11924.33	3734.632
2	22335		12089		14918		16447.33	4320.437
4	28241		17373		18883		21499	4807.005
8	33747		21523		25272		26847.33	5113.237
24	43075		29114		37832		36673.66	8758.106
48	50468		45791		37199		44486	5495.080
72	58708		56055		41221		51994.66	7694.739

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 05/09/91
File: SCMSTA45.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate AHH's H.N. 010181-PPDS2 6 MONTH @ 45 C/90% RH

STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC	Hr.
0	0	0	0	0.0
100	692161	635665	663913	0.5
500	3130083	3112454	3121269	1
800	4897447	4849777	4873612	2
1000	6190564	6329491	6260028	4
				8
				24
				48
				72

Data of Average Values

mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0
77.3	77.3	218.9	218.9
106.4	107.5	304.3	85.4
146.9	148.5	420.3	116.0
226.8	229.0	648.0	227.7
287.7	291.1	823.9	175.9
425.1	429.5	1215.4	391.5
542.7	549.1	1554.0	338.7
568.2	576.3	1631.0	77.0

Regression Output:

Constant	15908.43	6 MONTH STABILITY
Std Err of Y Est	65650.93	45 C/90% RH
R Squared	0.999548	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 6183.032
Std Err of Coef. 75.90845

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	477376	509003	496008	494129	12979.85
1	602138	721393	697094	673541.6	51455.30
2	838264	1052769	881954	924329	92555.67
4	1274300	1551572	1428279	1418050.	113426.6
8	1671558	1766135	1947176	1794956.	114351.2
24	2307415	3014579	2611656	2644550	289633.9
48	3201852	3523128	3390159	3371713	131807.3
72	3420446	3749168	3417384	3528999.	155687.7

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 95/10/31
File: CGMSTA45.WK1

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 910181-PDDS2 [illegible] Month Stability @ 38 C/

STANDARD CALIBRATION CURVE
= 254 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
1	894	980	937
10	10153	10276	10215
25	27109	25930	26520
50	55408	55359	55384

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	7.3	7.3	20.7	20.7
1	9.9	9.9	28.0	7.3
2	13.6	13.7	38.8	10.8
4	17.3	17.5	49.6	10.8
8	22.1	22.4	63.4	13.8
24	33.0	33.4	94.5	31.0
48	41.2	41.7	117.9	23.5
72	47.3	47.9	135.5	17.6

Regression Output:

Constant	-439.341	6 MONTH STABILITY
Std Err of Y Est	625.6089	38 C/90% RH
R Squared	0.999452	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 1107.572
Std Err of Coef. 14.96860

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	7056	8931	6944	7643.666	911.4297
1	9724	11493	9973	10396.66	781.3611
2	13625	16264	13905	14598	1183.572
4	17367	20775	17543	18761.66	1434.126
8	23338	25570	23367	24091.66	1045.406
24	35840	38014	34620	36158	1403.721
48	44546	48774	42169	45163	3731.546
72	49101	53515	53085	51900.33	1987.196

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 05/09/91
File: S6MSTA45.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PPDS2 6 MONTH @ 38C/30% RH

STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	692161	635665	663913
500	3130083	3112454	3121269
800	4897447	4849777	4873612
1000	6190564	6329491	6260028

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	77.8	77.8	220.2	220.2
1	119.9	121.1	342.7	122.5
2	171.1	172.9	489.3	146.6
4	249.6	252.2	713.7	224.4
8	352.7	356.5	1008.8	295.2
24	494.7	500.0	1414.3	406.1
48	589.7	597.1	1689.9	274.9
72	622.1	630.3	1785.5	95.7

Regression Output:

Constant	15908.43	6 MONTH STABILITY
Std Err of Y Est	65650.93	38 C/ 30% RH
R Squared	0.999548	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 6183.032
Std Err of Coef. 75.90845

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	450672	595538	445016	497082	69671.32
1	781544	841883	748817	757414.6	65739.83
2	1076189	1114790	1030436	1073805	34478.61
4	1509339	1629562	1538920	1559293.	51127.95
8	2242327	2267682	2080666	2196891.	82833.25
24	3044218	3192014	2987526	3074586	86199.37
48	3753571	3677682	3555076	3662109.	81779.94
72	3822112	4001768	3763025	3862301.	101524.9

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 05/20/91
File: CGMSTA38.WK1

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010191-PDDS2 6 Month Stability @ RT

STANDARD CALIBRATION CURVE
= 254 nm

mcg/ml	ACC	AUC	AVGAUC
0	0	0	0
1	894	980	937
10	10153	10276	10215
25	27109	25930	26520
50	55408	55359	55384

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	4.0	4.0	11.3	11.3
1	5.3	5.4	15.2	4.0
2	7.3	7.4	20.9	5.7
4	10.0	10.1	28.6	7.7
8	12.6	12.8	36.1	7.5
24	14.7	14.8	42.0	5.9
48	20.1	20.3	57.6	15.6
72	22.3	22.6	63.8	6.3

Regression Output:

Constant	-439.341	6 MONTH STABILITY
Std Err of Y Est	625.6089	ROOM TEMPERATURE
R Squared	0.999452	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 1107.572
Std Err of Coef. 14.96860

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	4363	3911	3625	3966.333	303.8171
1	5555	5516	5277	5449.333	122.8938
2	7818	3042	7346	7668.666	286.3905
4	10256	10196	11478	10643.33	530.7065
8	13605	13908	13064	13525.66	343.9982
24	16729	14897	15762	15796	748.2971
48	21975	21373	22204	21850.66	350.4609
72	24769	23532	24337	24212.66	512.5988

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 05/09/91
File: SGMSTA45.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PPDS2 6 MONTH @ RT

STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	692161	635665	663913
500	3130083	3112454	3121269
800	4897447	4849777	4873612
1000	6190564	6329491	6260028

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	105.2	105.2	297.8	297.8
1	140.7	142.3	402.6	104.8
2	202.7	204.8	579.6	177.0
4	297.5	300.5	850.4	270.8
8	426.6	431.1	1220.0	369.6
24	552.3	558.7	1581.1	361.1
48	731.3	739.6	2093.0	511.9
72	768.1	779.0	2204.6	111.6

Regression Output:

Constant	15908.43	6 MONTH STABILITY
Std Err of Y Est	65650.93	ROOM TEMPERATURE
R Squared	0.999548	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 6183.032
Std Err of Coef. 75.90845

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	708546	593068	698189	666601	52167.31
1	930059	818214	909176	885816.3	48556.36
2	1269039	1225863	1312593	1269165	35407.48
4	1896005	1783092	1886331	1855142.	51100.36
8	2777645	2469644	2714035	2653774.	132764.5
24	3495444	3155994	3640825	3430754.	203148.2
48	4619820	4415922	4576798	4537513.	87753.67
72	4910904	4537627	4845923	4764818	162823.9

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 05/22/91
File: CGMSTART.WK1

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PDDS2 6 Month Stability 23 C/ W

STANDARD CALIBRATION CURVE
= 254 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
1	894	980	937
10	10153	10276	10215
25	27109	25930	26520
50	55408	55359	55384

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	3.7	3.7	10.4	10.4
1	5.1	5.2	14.6	4.2
2	7.4	7.5	21.1	6.5
4	9.5	9.7	27.3	6.2
8	12.3	12.4	35.1	7.8
24	14.0	14.2	40.1	5.0
48	18.9	19.1	54.0	13.9
72	19.5	19.8	56.0	2.0

Regression Output:

Constant	-439.341	6 MONTH STABILITY
Std Err of Y Est	625.6089	23 C UNDER WATER
R Squared	0.999452	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 1107.572
Std Err of Coef. 14.96860

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	3486	4220	3228	3644.666	420.2359
1	4850	5436	5407	5231	269.6676
2	7152	8035	8033	7740	415.7795
4	9549	10684	10146	10126.33	483.5704
8	13469	13800	12161	13143.33	707.6365
24	15678	18223	11304	15068.33	2857.377
48	19521	21045	20847	20471	676.5973
72	22036	18746	22748	21176.66	1743.146

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 05/15/91
File: S6MSTAWT.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PPDS2 6 MONTH @ 23C/WATER

STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	692161	635665	663913
500	3130083	3112454	3121269
800	4897447	4849777	4873612
1000	6190564	6329491	6260028

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	80.7	80.7	228.5	228.5
1	124.8	126.9	356.6	128.1
2	188.2	190.1	537.3	181.3
4	286.5	289.3	818.7	280.8
8	423.3	427.6	1210.2	391.5
24	606.2	612.5	1733.5	523.3
48	685.8	694.9	1966.8	233.1
72	689.9	700.2	1981.5	14.7

Regression Output:

Constant	15908.43	6 MONTH STABILITY
Std Err of Y Est	65650.93	23 C UNDER WATER
R Squared	0.999548	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 6183.032
Std Err of Coef. 75.90845

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	444615	533168	567477	515086.6	51762.07
1	722698	804295	835640	787544.3	47605.40
2	1132859	1277463	1128383	1179568.	69246.09
4	1685726	1924886	1750713	1787108.	100971.4
8	2423399	2966011	2510888	2633432.	237865.2
24	3587015	4159009	3546150	3764058	279770.3
48	3964894	4548781	4255231	4256295.	238363.3
72	4168673	4548004	4127929	4281535.	189154.5

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 05/22/91
File: CGMSTAWT.WK1

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PDDS2 6 Month Stability -40 C

STANDARD CALIBRATION CURVE
= 254 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
1	894	980	937
10	10153	10276	10215
25	27109	25930	26520
50	55408	55359	55384

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	3.8	3.8	10.7	10.7
1	4.2	4.3	12.2	1.5
2	5.9	6.0	16.9	4.8
4	6.7	6.8	19.3	2.4
8	7.6	7.7	21.7	2.5
24	10.7	10.8	30.5	8.8
48	13.7	13.8	39.1	8.6
72	13.7	13.9	39.3	0.2

Regression Output:

Constant	-439.341	6 MONTH STABILITY
Std Err of Y Est	625.6089	-40 C
R Squared	0.999452	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 1107.572
Std Err of Coef. 14.96860

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	4459	2535	4195	3729.666	851.6044
1	4533	4087	4149	4256.333	197.2635
2	5893	6074	6376	6114.333	199.2357
4	7748	7343	5929	7006.666	779.7565
8	9069	6692	8122	7961	977.0612
24	14519	9713	9897	11376.33	2223.470
48	15948	16874	11246	14689.33	2463.977
72	11812	19031	13307	14716.66	3111.147

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 05/09/91
File: SGMSTA45.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PPDS2 6 MONTH @ -40C

STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	692161	635665	663913
500	3130083	3112454	3121269
800	4897447	4849777	4873612
1000	6190564	6329491	6260028

Data of Average Values

Hr.	mcg/ml	dil adj mcg/ml	mcg/cm2	dif u/cm2
0.0	0.0	0.0	0.0	0.0
0.5	75.7	75.7	214.2	214.2
1	109.9	111.0	314.2	100.1
2	172.6	174.2	493.0	178.8
4	258.7	261.3	739.4	246.4
8	355.5	359.4	1017.0	277.6
24	499.3	504.7	1428.2	411.1
48	616.7	624.2	1766.3	338.2
72	666.6	675.9	1912.7	146.3

Regression Output:

Constant	15908.43	6 MONTH STABILITY
Std Err of Y Est	65650.93	-40 C
R Squared	0.999548	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 6183.032
Std Err of Coef. 75.90845

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	430592	541283	479739	483864.6	45275.33
1	635802	836985	613601	695462.6	100481.0
2	1016469	1213339	1018920	1082909.	92233.12
4	1501246	1827199	1517610	1615351.	149947.5
8	2244228	2427895	1969804	2213975.	188234.3
24	3548582	3047262	2713832	3103225.	343075.1
48	3955589	4328524	3202116	3828743	468519.7
72	4134969	4581666	3696127	4137587.	361524.5

Formulation	Wt.%
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 05/20/91
File: CGMSTA40.WK1
